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L2 ANSWER 1 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:423734 CAPLUS
TITLE: **Stable lansoprazole** formulation
INVENTOR(S): Avramoff, Avi; Azoulay, Valerie
PATENT ASSIGNEE(S): Dexcel, Ltd., Israel; Graeser, D'vorah
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005044240	A2	20050519	WO 2004-US32775	20041101

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-515672P P 20031031

AB A **stable** composition comprising a substrate comprising lansopraxole (preferably in the base form), without any alkaline agent; a subcoating layer containing alkaline agent; and an enteric coating layer. The substrate is preferably as inert core with an active layer (containing lansopraxole) layered over it.

TI **Stable lansoprazole** formulation

AB A **stable** composition comprising a substrate comprising lansopraxole (preferably in the base form), without any alkaline agent; a

subcoating layer containing alkaline agent; and an enteric coating layer. The substrate is preferably as inert core with an active layer (containing lansopraxole) layered over it.

L2 ANSWER 2 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:281759 CAPLUS
DOCUMENT NUMBER: 142:341903
TITLE: Pharmaceutical compositions of benzimidazole and processes for their preparation
INVENTOR(S): Singh, Romi Barat; Kumar, Pananchukunnath Manoj; Nagaprasad, Vishnubhotla; Sethi, Sanjeev Kumar; Malik, Rajiv
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027876	A1	20050331	WO 2004-IB2784	20040827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004075881	A1	20040910	WO 2004-IB536	20040301
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:
IN 2003-DE1047 A 20030828
WO 2004-IB536 A 20040301
IN 2003-DE203 A 20030228

AB The tech. field of the present invention relates to **stable** pharmaceutical compns. of acid-labile benzimidazole derivative using increased amts. of low-viscosity hydroxypropylcellulose, and processes for the preparation of these compns. The pharmaceutical composition includes one or more cores. The cores include an acid-labile benzimidazole derivative and at least 10% weight/weight of low-viscosity hydroxypropylcellulose by weight of the benzimidazole derivative

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The tech. field of the present invention relates to **stable** pharmaceutical compns. of acid-labile benzimidazole derivative using increased

amts. of low-viscosity hydroxypropylcellulose, and processes for the preparation of these compns. The pharmaceutical composition includes one or more cores. The cores include an acid-labile benzimidazole derivative and at least 10% weight/weight of low-viscosity hydroxypropylcellulose by weight of the benzimidazole derivative

IT 51-17-2D, Benzimidazole, derivs. 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 104340-86-5, Leminoprazole 117976-89-3, Rabeprazole 117976-90-6, Pariprazole 119141-88-7, Esomeprazole 138786-67-1, Pantoprazole sodium
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmaceutical compns. of benzimidazole)

L2 ANSWER 3 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:99343 CAPLUS
DOCUMENT NUMBER: 142:162692
TITLE: Pharmaceutical compositions having a swellable coating
INVENTOR(S): Srinivas, Irukulla; Dixit, Akhilesh Ashok; Reddy, Pallempalli Venkata Siva; Reddy, Billa Praveen; Mohan, Mailatur Sivaraman; Ravinder, Kodipyaka; Nasare, Vijay; Pergament, Edward D.
PATENT ASSIGNEE(S): Reddy's Laboratories, Inc., USA; Reddy's Laboratories Ltd
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005009410	A2	20050203	WO 2004-US22910		20040716
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2005042277	A1	20050224	US 2004-893563		20040716
PRIORITY APPLN. INFO.:			IN 2003-CH580	A	20030717
			IN 2003-CH1064	A	20031230
			US 2004-563707P	P	20040420

AB A pharmaceutical dosage form containing an active agent that is not **stable** in the presence of an acid comprises a core containing the active and a disintegrant, a swellable coating surrounding the core, and an enteric coating surrounding the swellable coating. Thus, core pellets contained omeprazole 40, mannitol 236, Crospovidone 18, HPMC 8, Ploxamer-407 5, and meglumine 3, mg/capsule. A swellable coating composition comprised Zein F6000 2 mg. The enteric coating contained HPMC phthalate 63.24, tri-Et citrate 6.31 and talc 9.45 mg/capsule.

AB A pharmaceutical dosage form containing an active agent that is not **stable** in the presence of an acid comprises a core containing the active and a disintegrant, a swellable coating surrounding the core, and an enteric coating surrounding the swellable coating. Thus, core pellets

contained omeprazole 40, mannitol 236, Crospovidone 18, HPMC 8, Ploxamer-407 5, and meglumine 3, mg/capsule. A swellable coating composition comprised Zein F6000 2 mg. The enteric coating contained HPMC phthalate 63.24, tri-Et citrate 6.31 and talc 9.45 mg/capsule.

IT 50-00-0D, Formaldehyde, casein conjugates, biological studies 51-17-2D, Benzimidazole, derivs. 88-12-0D, polymers 471-34-1, Calcium carbonate, biological studies 497-19-8, Sodium carbonate, biological studies 9000-69-5, Pectin 9002-18-0, Agar 9003-39-8, Polyvinylpyrrolidone 9004-34-6D, Cellulose, derivs. 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 10103-46-5, Calcium phosphate 25212-88-8, Ethyl acrylate-methacrylic acid copolymer 53237-50-6 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 117976-89-3, Rabeprazole 117976-90-6, Rabeprazole sodium 119141-88-7, Esomeprazole 138786-67-1, Pantoprazole sodium 164579-32-2, Pantoprazole sodium sesquihydrate 217087-09-7, Esomeprazole magnesium trihydrate 226904-39-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. having swellable coating)

L2 ANSWER 4 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1005301 CAPLUS
DOCUMENT NUMBER: 142:246134
TITLE: Method of making oral preparation of omeprazole
INVENTOR(S): Hong, Seok Cheon; Kil, Yeong Sik
PATENT ASSIGNEE(S): Korea United Pharm. Inc., S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2003039707	A	20030522	KR 2001-70733	20011114

PRIORITY APPLN. INFO.: KR 2001-70733 20011114

AB An oral preparation containing omeprazole is provided which is pharmaceutically **stable** by prevention of the loss of activity of omeprazole caused by gastric acid when orally administered and facilitating the absorption thereof into the small intestine, thereby maximizing therapeutic effect. In a method of making an oral preparation, non-volatile minute granules with a particle size of 0.2-0.7 mm are first made using starch and sugar, or only sugar. Then, omeprazole or **lansoprazole** and the salt thereof, and a binder selected from hydroxy Pr Me cellulose or hydroxy Pr cellulose and derivs. thereof are dissolved or diffused in a solvent containing a mixture of purified water, acetone and ethanol. The resulting solution, and the minute granules are mixed together with talc. The mixture is coated by a protection film to produce a pellet having a diameter of 0.3-2.5 mm.

AB An oral preparation containing omeprazole is provided which is pharmaceutically **stable** by prevention of the loss of activity of omeprazole caused by gastric acid when orally administered and facilitating the absorption thereof into the small intestine, thereby maximizing therapeutic effect. In a method of making an oral preparation, non-volatile minute granules with a particle size of 0.2-0.7 mm are first made using starch and sugar, or only sugar. Then, omeprazole or **lansoprazole** and the salt thereof, and a binder selected from hydroxy Pr Me cellulose or hydroxy Pr cellulose and derivs. thereof are dissolved or diffused in a solvent containing a mixture of purified water, acetone and ethanol. The resulting solution, and the minute granules are mixed together with talc. The mixture is coated by a protection film to produce a pellet having a diameter of 0.3-2.5 mm.

IT 9004-64-2, Hydroxy propyl cellulose 9004-65-3, Hydroxy propyl methyl

cellulose 14807-96-6, Talc, biological studies 73590-58-6, Omeprazole 103577-45-3, **Lansoprazole**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(making oral preparation of omeprazole)

L2 ANSWER 5 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:995952 CAPLUS
DOCUMENT NUMBER: 141:416020
TITLE: An improved and **stable** pharmaceutical composition containing substituted benzimidazoles
INVENTOR(S): Venkaiah, Chowdary Nannapaneni; Khadgapathi, Podili; Ramarao, Pendyala
PATENT ASSIGNEE(S): Natco Pharma Limited, India
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098573	A1	20041118	WO 2003-IN179	20030508

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2003-IN179 20030508

AB The present invention relates to improved pharmaceutical prepns. containing substituted benzimidazoles,(i.e.omeprazole, **lansoprazole**, pantoprazole, and rabeprazole). The prepns. comprise an inert core, constituted by starch and sugar, surrounded by active coating containing at least one substituted benzimidazole in the micronized form, which is mixed with pharmaceutically acceptable non-alkaline and inert excipients, followed by intermediate coating and an enteric coating, in order to guarantee the integrity of the product until it reaches the proximal part of the small intestine, where the formulation will be disaggregated to facilitate the absorption of the substituted benzimidazole compound

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI An improved and **stable** pharmaceutical composition containing substituted benzimidazoles

AB The present invention relates to improved pharmaceutical prepns. containing substituted benzimidazoles,(i.e.omeprazole, **lansoprazole**, pantoprazole, and rabeprazole). The prepns. comprise an inert core, constituted by starch and sugar, surrounded by active coating containing at least one substituted benzimidazole in the micronized form, which is mixed with pharmaceutically acceptable non-alkaline and inert excipients, followed by intermediate coating and an enteric coating, in order to guarantee the integrity of the product until it reaches the proximal part of the small intestine, where the formulation will be disaggregated to facilitate the absorption of the substituted benzimidazole compound

ST benzimidazole pharmaceutical **stable**

IT Drug delivery systems
(capsules; improved and **stable** pharmaceutical composition containing substituted benzimidazoles)

IT Drug delivery systems
(granules, enteric-coated; improved and **stable** pharmaceutical composition containing substituted benzimidazoles)
IT Castor oil
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrogenated; improved and **stable** pharmaceutical composition containing substituted benzimidazoles)
IT Antiulcer agents
Plasticizers
Ulcer
(improved and **stable** pharmaceutical composition containing substituted benzimidazoles)
IT Polyoxyalkylenes, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(improved and **stable** pharmaceutical composition containing substituted benzimidazoles)
IT 57-11-4, Stearic acid, biological studies 57-50-1, Sucrose, biological studies 63-42-3, Lactose 69-65-8, D-Mannitol 84-66-2, Diethyl phthalate 84-74-2, Dibutyl phthalate 112-92-5, Stearyl alcohol 117-81-7, Dioctyl phthalate 131-16-8, Dipropyl phthalate 151-21-3, Sodium lauryl sulfate, biological studies 577-11-7, Dioctyl sodium sulfosuccinate 7757-93-9, Dicalcium phosphate 9000-11-7, CM cellulose 9003-39-8, Pvp 9004-32-4 9004-34-6, Cellulose, biological studies 9004-38-0, Cellulose acetate phthalate 9004-62-0, Hydroxyethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hpmc 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 9050-31-1, Hydroxypropyl methyl cellulose phthalate 13463-67-7, Titania, biological studies 14807-96-6, Talc, biological studies 25212-88-8, Eudragit L-100-55 25322-68-3, Peg 36653-82-4, Cetyl alcohol
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(improved and **stable** pharmaceutical composition containing substituted benzimidazoles)
IT 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 117976-89-3, Rabeprazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(improved and **stable** pharmaceutical composition containing substituted benzimidazoles)

L2 ANSWER 6 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:965061 CAPLUS
DOCUMENT NUMBER: 141:400968
TITLE: Pellet formulations of acid-labile antiulcer benzimidazole compounds
INVENTOR(S): Carvajal Martin, Luis; Asensio Asensio, Juan Carlos; Sevilla Tirado, Francisco Javier
PATENT ASSIGNEE(S): Laboratorios Belmac, S.A., Spain
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096218	A2	20041111	WO 2004-EP50618	20040427
WO 2004096218	A3	20050506		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG
PRIORITY APPLN. INFO.: ES 2003-976 A 20030429
OTHER SOURCE(S): MARPAT 141:400968
AB The formulations comprise inert granules of sugar/starch which are: initially coated with a non-alkaline active layer having the benzimidazole compound (omeprazole, **lansoprazole**, pantoprazole, rabeprazole, etc.), sodium and/potassium salts of acids of formula R-O-SO3H wherein R is an alkyl radical of a (C6-C20)-fatty acid (preferably sodium lauryl sulfate), (C6-C20)-fatty acids (preferably oleic acid), sodium and/or potassium salts Of (C6-C20)-fatty acids (preferably potassium oleate), sodium carboxymethyl starch and polyvinylpyrrolidone; secondly coated with a non-alkaline barrier layer having hydroxypropylmethylcellulose; and finally coated with an enteric layer. The preferred molar ratio (sodium lauryl sulfate):(oleic acid + potassium oleate) is between 4:1 and 6:1. All coatings are done with aqueous solns., suspensions or dispersions at a relatively high temperature, and all dryings are done at a relatively low temperature and for a relatively short time. They are **stable** over time and useful for oral administration.
AB The formulations comprise inert granules of sugar/starch which are: initially coated with a non-alkaline active layer having the benzimidazole compound (omeprazole, **lansoprazole**, pantoprazole, rabeprazole, etc.), sodium and/potassium salts of acids of formula R-O-SO3H wherein R is an alkyl radical of a (C6-C20)-fatty acid (preferably sodium lauryl sulfate), (C6-C20)-fatty acids (preferably oleic acid), sodium and/or potassium salts Of (C6-C20)-fatty acids (preferably potassium oleate), sodium carboxymethyl starch and polyvinylpyrrolidone; secondly coated with a non-alkaline barrier layer having hydroxypropylmethylcellulose; and finally coated with an enteric layer. The preferred molar ratio (sodium lauryl sulfate):(oleic acid + potassium oleate) is between 4:1 and 6:1. All coatings are done with aqueous solns., suspensions or dispersions at a relatively high temperature, and all dryings are done at a relatively low temperature and for a relatively short time. They are **stable** over time and useful for oral administration.
IT 73590-58-6P, Omeprazole 103577-45-3P, **Lansoprazole**
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(pellet formulations of acid-labile antiulcer benzimidazole compds.)

L2 ANSWER 7 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:942454 CAPLUS
DOCUMENT NUMBER: 142:155949
TITLE: Modification and purification method of crystalline form of **lansoprazole**
INVENTOR(S): Ahn, Hyeon Suk; Baek, Yong Gu; Jang, Dong Jo; Kim, Gyeong Su; Kim, Min Su; Kim, Sang Hun; Kim, Wan Ju; Lee, Dong U.; Park, Seong Jun; Yoo, Jeong Bok
PATENT ASSIGNEE(S): C-Tri, S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent

LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2003000779	A	20030106	KR 2001-36898	20010627

PRIORITY APPLN. INFO.: KR 2001-36898 20010627

AB Provided is a modification and purification method of **Lansoprazole** (crystal form II) into **Lansoprazole** (crystal form I) which is thermodynamically **stable** and is used as a drug. **Lansoprazole**, represented by the formula(I), is an inhibitor of proton pump (anti-ulcer agent), has strong antibacterial activity and excellent pharmacol. activity, and is thus useful as a therapeutic agent for stomach ulcer. The method comprises the steps of: mixing 1 weight% of **Lansoprazole** (crystal form II) and 1-100 weight% of an organic solvent; filtering the mixture; and drying the filtrate. The solvent is selected from the groups of ester containing Me acetate and Et acetate; halogenated hydrocarbon such as methylene chloride and chloroform; ethers including THF, Et ether, iso-Pr ether and petroleum ether; hydrocarbons with more than 5 carbons such as pentane, hexane, heptane cyclohexane; nitriles such as acetonitrile; ketones such as acetone; and a mixture thereof.

TI Modification and purification method of crystalline form of **lansoprazole**

AB Provided is a modification and purification method of **Lansoprazole** (crystal form II) into **Lansoprazole** (crystal form I) which is thermodynamically **stable** and is used as a drug. **Lansoprazole**, represented by the formula(I), is an inhibitor of proton pump (anti-ulcer agent), has strong antibacterial activity and excellent pharmacol. activity, and is thus useful as a therapeutic agent for stomach ulcer. The method comprises the steps of: mixing 1 weight% of **Lansoprazole** (crystal form II) and 1-100 weight% of an organic solvent; filtering the mixture; and drying the filtrate. The solvent is selected from the groups of ester containing Me acetate and Et acetate; halogenated hydrocarbon such as methylene chloride and chloroform; ethers including THF, Et ether, iso-Pr ether and petroleum ether; hydrocarbons with more than 5 carbons such as pentane, hexane, heptane cyclohexane; nitriles such as acetonitrile; ketones such as acetone; and a mixture thereof.

ST **lansoprazole** cryst form prepn antiulcer agent antibacterial agent

IT Antibacterial agents
Antiulcer agents
(of crystalline form of **lansoprazole**)

IT 103577-45-3P, **Lansoprazole**
RL: PUR (Purification or recovery); PREP (Preparation)
(preparation of crystalline form of **lansoprazole**)

L2 ANSWER 8 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:878281 CAPLUS
DOCUMENT NUMBER: 141:355384
TITLE: A **stable** oral benzimidazole formulation
INVENTOR(S): Desai, Jatin; Patel, Pankaj Ramanbhai; Veerababu, Ramabrahammam T.; Jogani, Pranav
PATENT ASSIGNEE(S): Cadila Healthcare Limited, India
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2004089333	A2	20041021	WO 2004-IN50 20040226
WO 2004089333	A3	20050203	

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IN 2003-MU237 A 20030228

AB A **stable** oral pharmaceutical composition comprising a benzimidazole compound or its pharmaceutically acceptable salt is described, wherein the active ingredient is coated with an enteric coating polymer and has no separating or protective layer in between. These pellets can be filled into the capsules or compressed into tablets. Further, a method for the manufacture of such a formulation, and the use of such a formulation in medicine is disclosed. For example, sugar beads (1000 g) were coated with a composition containing omeprazole 200 g, hydroxypropyl Me cellulose 240 g, talc 200 g, and water as needed to form pellets. Pellets (500 g) were then enteric coated with a composition containing Eudragit L30D-55 690 g, tri-Et citrate 19.15 g, talc 24.24 g, 30% ammonia solution as needed for pH 4.5 to 5.5, and water as needed. The coated pellets can be filled in hard gelatin capsules. When tested 99.3 to 100% drug was released within 30 min. The unit dose pellets contained less than 0.7% related substances. The gastro-resistance was found to be 1.81%.

TI A **stable** oral benzimidazole formulation

AB A **stable** oral pharmaceutical composition comprising a benzimidazole compound or its pharmaceutically acceptable salt is described, wherein the active ingredient is coated with an enteric coating polymer and has no separating or protective layer in between. These pellets can be filled into the capsules or compressed into tablets. Further, a method for the manufacture of such a formulation, and the use of such a formulation in medicine is disclosed. For example, sugar beads (1000 g) were coated with a composition containing omeprazole 200 g, hydroxypropyl Me cellulose 240 g, talc 200 g, and water as needed to form pellets. Pellets (500 g) were then enteric coated with a composition containing Eudragit L30D-55 690 g, tri-Et citrate 19.15 g, talc 24.24 g, 30% ammonia solution as needed for pH 4.5 to 5.5, and water as needed. The coated pellets can be filled in hard gelatin capsules. When tested 99.3 to 100% drug was released within 30 min. The unit dose pellets contained less than 0.7% related substances. The gastro-resistance was found to be 1.81%.

IT Glycerides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C12-18, polymers with ethylene glycol; preparation of **stable** benzimidazole enteric-coated oral formulations)

IT Monoglycerides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C18-unsatd., polymers with ethylene glycol; preparation of **stable** benzimidazole enteric-coated oral formulations)

IT Glycerides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C8-10, ethoxylated, solubilizer; preparation of **stable** benzimidazole enteric-coated oral formulations)

IT Carbohydrates, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(beads, cores; preparation of **stable** benzimidazole enteric-coated

oral formulations)
IT Drug delivery systems
(capsules, enteric-coated; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT Castor oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ethoxylated, Cremophore EL, solubilizer; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT Glycerides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medium-chain, solubilizer; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT Drug delivery systems
(pellets, enteric-coated; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT Gums and Mucilages
Plasticizers
Solubilizers
(preparation of **stable** benzimidazole enteric-coated oral formulations)
IT Glycerides, biological studies
Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **stable** benzimidazole enteric-coated oral formulations)
IT Drug delivery systems
(tablets, enteric-coated; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT 9003-39-8D, crosslinked
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Crospovidone; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT 9005-25-8, Starch, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cores; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT 79-41-4D, Methacrylic acid, esters, polymers 9004-38-0, Cellulose acetate phthalate 9010-88-2, Ethyl acrylate-methyl methacrylate copolymer 9050-31-1, Hydroxypropyl methyl cellulose phthalate 25212-88-8, Eudragit L30D-55 37205-99-5, Carboxymethyl ethyl cellulose 53237-50-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteric coating; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT 9004-34-6, Cellulose, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcryst., cores; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT 77-93-0, Triethyl citrate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(plasticizer; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT 51-17-2D, Benzimidazole, compds. 57-50-1, Sucrose, biological studies 4070-80-8, Sodium stearyl fumarate 9003-39-8, Polyvinylpyrrolidone 9004-32-4, Carboxymethyl cellulose sodium 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9005-65-6, Tween 80 25322-68-3, Polyethylene glycol 31566-31-1, Glyceryl monostearate 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, Lansoprazole 117976-89-3, Rabeprazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **stable** benzimidazole enteric-coated oral formulations)

IT 151-21-3, Sodium lauryl sulfate, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solubilizer; preparation of **stable** benzimidazole enteric-coated oral formulations)

L2 ANSWER 9 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:834106 CAPLUS
DOCUMENT NUMBER: 142:397408
TITLE: Preparation and evaluation of inclusion complex of **lansoprazole** with 2-HP-β-cyclodextrin and meglumine
AUTHOR(S): Lee, Jung Woo; Kim, Jung Su; Chang, Hye Jin; Lee, Gye Won; Jee, Ung Kil
CORPORATE SOURCE: College of Pharmacy, Chungnam National University, Daejeon, 305-764, S. Korea
SOURCE: Yakche Hakhoechi (2004), 34(4), 269-274
CODEN: YAHAEX; ISSN: 0259-2347
PUBLISHER: Korean Society of Pharmaceutics
DOCUMENT TYPE: Journal
LANGUAGE: Korean

AB To enhance the solubility and stability of **lansoprazole** (LAN), new proton pump inhibitor, we were prepared various molar ratio of inclusion complex with 2-hydroxypropyl-β-cyclodextrin (HPCD) and organic alkali agent, meglumine (MEG). Inclusion complex formation of LAN with HPCD was investigated by Differential Scanning Calorimetry and X-ray diffractometry. The aqueous solubilities of inclusion complexes, and the stabilities of 1:4 and 1:5 inclusion complexes in aqueous solns. containing different concns. of MEG were examined The stability of 1:5 LAN-HPCD inclusion complex containing MEG, which was equaled to amount of LAN, was performed in 0.9% NaCl and 5% dextrose solution The formation of inclusion complex of LAN with HPCD was AL type and the molar ratio of complex was 1:1. The stability constant was 41.557 M-1. As molar ratio of LAN to HPCD was increased, solubility of inclusion complex was increased. 1:5 LAN-HPCD inclusion complex was more **stable** than 1:4 LAN-HPCD inclusion complex. And as contained MEG amount in LAN solution was increased, stability of 1:4 and 1:5 LAN-HPCD inclusion complexes was improved. Also stability of 1:5 LAN-HPCD-MEG inclusion complex in 0.9% NaCl solution and 5% dextrose solution was similar to it in water at room temperature, but it was unstable at 40°C.

TI Preparation and evaluation of inclusion complex of **lansoprazole** with 2-HP-β-cyclodextrin and meglumine

AB To enhance the solubility and stability of **lansoprazole** (LAN), new proton pump inhibitor, we were prepared various molar ratio of inclusion complex with 2-hydroxypropyl-β-cyclodextrin (HPCD) and organic alkali agent, meglumine (MEG). Inclusion complex formation of LAN with HPCD was investigated by Differential Scanning Calorimetry and X-ray diffractometry. The aqueous solubilities of inclusion complexes, and the stabilities of 1:4 and 1:5 inclusion complexes in aqueous solns. containing different concns. of MEG were examined The stability of 1:5 LAN-HPCD inclusion complex containing MEG, which was equaled to amount of LAN, was performed in 0.9% NaCl and 5% dextrose solution The formation of inclusion complex of LAN with HPCD was AL type and the molar ratio of complex was 1:1. The stability constant was 41.557 M-1. As molar ratio of LAN to HPCD was increased, solubility of inclusion complex was increased. 1:5 LAN-HPCD inclusion complex was more **stable** than 1:4 LAN-HPCD inclusion complex. And as contained MEG amount in LAN solution was increased, stability of 1:4 and 1:5 LAN-HPCD inclusion complexes was improved. Also stability of 1:5 LAN-HPCD-MEG inclusion complex in 0.9% NaCl solution and 5% dextrose solution was similar to it in water at room temperature, but it was unstable at 40°C.

ST **lansoprazole** hydroxypropyl cyclodextrin inclusion complex meglumine soly

IT Drug delivery systems
(solns.; preparation and evaluation of inclusion complex of **lansoprazole** with 2-HP-β-cyclodextrin and meglumine)
IT 57-55-6DP, 1,2-Propanediol, cyclodextrin ethers, **lansoprazole** complexes 7585-39-9DP, β-Cyclodextrin, hydroxypropyl ethers, **lansoprazole** complexes 103577-45-3DP, **Lansoprazole**, complexes with hydroxypropyl cyclodextrin
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and evaluation of inclusion complex of **lansoprazole** with 2-HP-β-cyclodextrin and meglumine)
IT 6284-40-8, Meglumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and evaluation of inclusion complex of **lansoprazole** with 2-HP-β-cyclodextrin and meglumine)

L2 ANSWER 10 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:696366 CAPLUS
DOCUMENT NUMBER: 141:212763
TITLE: Method of stabilizing **lansoprazole**
INVENTOR(S): Singer, Claude; Liberman, Anita; Veinberg, Irena
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004072061	A1	20040826	WO 2004-US3603		20040205
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
EP 1485373	A1	20041215	EP 2004-708666		20040205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2005020638	A1	20050127	US 2004-773535		20040205
PRIORITY APPLN. INFO.:			US 2003-445219P	P	20030205
			WO 2004-US3603	W	20040205

AB The present invention provides a **stable** 2-(2-pyridylmethyl)sulfinyl-1H-benzimidazole (**lansoprazole**) and a method for stabilizing **lansoprazole** by use of a weakly basic material. The present invention also provides a method for the preparation of a **stable lansoprazole**. **Lansoprazole** was prepared by oxidation its thio analog and purified with a solution of EtOH, NH3, and water.
TI Method of stabilizing **lansoprazole**
AB The present invention provides a **stable** 2-(2-pyridylmethyl)sulfinyl-1H-benzimidazole (**lansoprazole**) and a

method for stabilizing **lansoprazole** by use of a weakly basic material. The present invention also provides a method for the preparation of a **stable lansoprazole. Lansoprazole** was prepared by oxidation its thio analog and purified with a solution of EtOH, NH3, and water.

ST **lansoprazole** stabilization purifn prepn

IT Crystallization
(stabilizing **lansoprazole**)

IT Acids, processes
Amines, processes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(stabilizing **lansoprazole**)

IT 131926-99-3P, 1H-Benzimidazole, 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfonyl-
RL: BYP (Byproduct); PREP (Preparation)
(stabilizing **lansoprazole**)

IT 64-17-5, Ethanol, processes 64-18-6, Formic acid, processes 64-19-7, Acetic acid, processes 67-56-1, Methanol, processes 67-63-0, 2-Propanol, processes 67-64-1, Acetone, processes 68-12-2, Dmf, processes 71-23-8, 1-Propanol, processes 74-89-5, Methylamine, processes 78-93-3, 2-Butanone, processes 102-71-6, Triethanolamine, processes 109-89-7, Diethylamine, processes 109-99-9, Thf, processes 111-42-2, Diethanolamine, processes 121-44-8, Triethylamine, processes 1336-21-6, Ammonium hydroxide 7647-01-0, Hydrochloric acid, processes 7664-41-7, Ammonia, processes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(stabilizing **lansoprazole**)

IT 103577-45-3P, **Lansoprazole**
RL: PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(stabilizing **lansoprazole**)

IT 103577-40-8, 1H-Benzimidazole, 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]thio-
RL: RCT (Reactant); RACT (Reactant or reagent)
(stabilizing **lansoprazole**)

L2 ANSWER 11 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:648368 CAPLUS
DOCUMENT NUMBER: 141:179632
TITLE: **Stable** oral benzimidazole compositions
INVENTOR(S): Mehta, Kamal; Mathur, Rajeev Shanker; Sethi, Sanjeev Kumar; Malik, Rajiv; Gandhi, Rajesh; Isloor, Shashikanth; Malik, Rajiv
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004066982	A1	20040812	WO 2004-IB235	20040202

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,

IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

PRIORITY APPLN. INFO.: IN 2003-DE80 A 20030131
IN 2003-DE728 A 20030527

AB The present invention relates to **stable** oral benzimidazole compns. and processes for their preparation The **stable** oral benzimidazole pharmaceutical composition includes a core, a separating layer, and an enteric coating. The core includes a benzimidazole compound, a substantially water-soluble material and, optionally excipients, wherein the core is not alkaline The separating layer surrounds the core and includes a substantially water-soluble material and, excipients. The enteric coating surrounds the separating layer. At least one of the core and the separating layer includes the substantially water-soluble material without any excipients. Thus, an enteric coating comprised Eudragit L30D55 114.39, PEG-300 3.43, talc 12.12, TiO2 4.04 mg and water qs.

TI **Stable** oral benzimidazole compositions

AB The present invention relates to **stable** oral benzimidazole compns. and processes for their preparation The **stable** oral benzimidazole pharmaceutical composition includes a core, a separating layer, and an enteric coating. The core includes a benzimidazole compound, a substantially water-soluble material and, optionally excipients, wherein the core is not alkaline The separating layer surrounds the core and includes a substantially water-soluble material and, excipients. The enteric coating surrounds the separating layer. At least one of the core and the separating layer includes the substantially water-soluble material without any excipients. Thus, an enteric coating comprised Eudragit L30D55 114.39, PEG-300 3.43, talc 12.12, TiO2 4.04 mg and water qs.

ST **Stable** oral benzimidazole pharmaceutical

IT Drug delivery systems
(capsules, enteric-coated; **stable** oral benzimidazole compns.)

IT Drug delivery systems
(enteric-coated; **stable** oral benzimidazole compns.)

IT Drug delivery systems
(oral; **stable** oral benzimidazole compns.)

IT Binders
Gums and Mucilages
Lubricants
(**stable** oral benzimidazole compns.)

IT Alditols
Carbohydrates, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** oral benzimidazole compns.)

IT Drug delivery systems
(tablets, enteric-coated; **stable** oral benzimidazole compns.)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(water-soluble; **stable** oral benzimidazole compns.)

IT 9004-34-6, Cellulose, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcryst.; **stable** oral benzimidazole compns.)

IT 50-70-4, Sorbitol, biological studies 50-99-7, Dextrose, biological studies 57-50-1, Sucrose, biological studies 63-42-3, Lactose 69-65-8, Mannitol 87-99-0, Xylitol 557-04-0 4070-80-8, Sodium stearyl fumarate 7631-86-9, Silica, biological studies 9000-01-5, Gum arabic 9000-65-1, Gum tragacanth 9003-39-8, Polyvinylpyrrolidone 9004-34-6D, Cellulose, derivs. 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9004-67-5 9005-25-8, Starch,

biological studies 9005-25-8D, Starch, derivs. 9063-38-1, Sodium starch glycolate 11138-66-2, Xanthan gum 14807-96-6, Talc, biological studies 25086-89-9, Vinyl acetate-vinylpyrrolidone copolymer 25212-88-8, Eudragit L30D 55 73590-58-6, Omeprazole 74811-65-7, Croscarmellose sodium 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 117976-89-3, Rabeprazole 198085-73-3, Pearlitol SD 200 444902-50-5, Acryl-Eze
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable oral benzimidazole compns.)

L2 ANSWER 12 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:565090 CAPLUS
DOCUMENT NUMBER: 141:111579
TITLE: Controlled release formulation comprising benzimidazole derivatives with increased stability
INVENTOR(S): Jee, Ung Kil; Hwang, Sung Joo; Park, Jin Kyu; Park, Kyung Lae; Moon, Young Girl; Kwon, Yong Jin
PATENT ASSIGNEE(S): Centurion, Inc., S. Korea
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058257	A1	20040715	WO 2003-KR659	20030402

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: KR 2002-87300 A 20021230

AB Disclosed is a controlled release formulation with increased stability and a method of preparation The controlled release formulation comprises a pellet including a benzimidazole derivative or a pharmaceutically acceptable salt thereof as an active ingredient and a cationic polymer, and at least one coating layer selected from an intermediate coating layer, a moisture-resistant coating layer and an enteric coating layer as an outer layer surrounding the pellet. The controlled release formulation electrostatically stabilizes benzimidazole derivs. or pharmaceutically acceptable salts thereof, and thus exhibits excellent resistance to acidic and aqueous environments. A composition was prepared containing chitosan, lansoprazole, Na lauryl sulfate Na H phosphate, Avicel PH-102, L-HPC LH11, mannitol, HPMC, HPMCP, and cetyl alc. to form controlled release pellets.
AB Disclosed is a controlled release formulation with increased stability and a method of preparation The controlled release formulation comprises a pellet including a benzimidazole derivative or a pharmaceutically acceptable salt thereof as an active ingredient and a cationic polymer, and at least one coating layer selected from an intermediate coating layer, a moisture-resistant coating layer and an enteric coating layer as an outer layer surrounding the pellet. The controlled release formulation electrostatically stabilizes benzimidazole derivs. or pharmaceutically acceptable salts thereof, and thus exhibits excellent resistance to acidic and aqueous environments. A composition was prepared containing chitosan,

lansoprazole, Na lauryl sulfate Na H phosphate, Avicel PH-102, L-HPC LH11, mannitol, HPMC, HPMCP, and cetyl alc. to form controlled release pellets.

ST controlled release pellet benzimidazole deriv **stable**

IT 103577-45-3, **Lansoprazole**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release formulation comprising benzimidazole derivs. with increased stability)

L2 ANSWER 13 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:453656 CAPLUS
DOCUMENT NUMBER: 141:116452
TITLE: Chemistry of Covalent Inhibition of the Gastric (H+, K+)-ATPase by Proton Pump Inhibitors
AUTHOR(S): Shin, Jai Moo; Cho, Young Moon; Sachs, George
CORPORATE SOURCE: Department of Physiology and Medicine, University of California, Los Angeles, CA, 90073, USA
SOURCE: Journal of the American Chemical Society (2004), 126(25), 7800-7811
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:116452

AB Proton pump inhibitors (PPIs), drugs that are widely used for treatment of acid related diseases, are either substituted pyridylmethylsulfinyl benzimidazole or imidazopyridine derivs. They are all prodrugs that inhibit the acid-secreting gastric (H+, K+)-ATPase by acid activation to reactive thiophiles that form disulfide bonds with one or more cysteines accessible from the exoplasmic surface of the enzyme. This unique acid-catalysis mechanism had been ascribed to the nucleophilicity of the pyridine ring. However, the data obtained here show that their conversion to the reactive cationic thiophilic sulfenic acid or sulfenamide depends mainly not on pyridine protonation but on a second protonation of the imidazole component that increases the electrophilicity of the C-2 position on the imidazole. This protonation results in reaction of the C-2 with the unprotonated fraction of the pyridine ring to form the reactive derivs. The relevant PPI pKa's were determined by UV spectroscopy of the benzimidazole or imidazopyridine sulfinylmethyl moieties at different medium pH. Synthesis of a relatively acid **stable** analog, N1-Me **lansoprazole**, allowed direct determination of both pKa values of this intact PPI allowing calcn. of the two pKa values for all the PPIs. These values predict their relative acid stability and thus the rate of reaction with cysteines of the active proton pump at the pH of the secreting parietal cell. The PPI accumulates in the secretory canaliculus of the parietal cell due to pyridine protonation then binds to the pump and is activated by the second protonation on the surface of the protein to allow disulfide formation.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Proton pump inhibitors (PPIs), drugs that are widely used for treatment of acid related diseases, are either substituted pyridylmethylsulfinyl benzimidazole or imidazopyridine derivs. They are all prodrugs that inhibit the acid-secreting gastric (H+, K+)-ATPase by acid activation to reactive thiophiles that form disulfide bonds with one or more cysteines accessible from the exoplasmic surface of the enzyme. This unique acid-catalysis mechanism had been ascribed to the nucleophilicity of the pyridine ring. However, the data obtained here show that their conversion to the reactive cationic thiophilic sulfenic acid or sulfenamide depends mainly not on pyridine protonation but on a second protonation of the imidazole component that increases the electrophilicity of the C-2

position on the imidazole. This protonation results in reaction of the C-2 with the unprotonated fraction of the pyridine ring to form the reactive derivs. The relevant PPI pKa's were determined by UV spectroscopy of the benzimidazole or imidazopyridine sulfinylmethyl moieties at different medium pH. Synthesis of a relatively acid **stable** analog, N1-Me **lansoprazole**, allowed direct determination of both pKa values of this intact PPI allowing calcn. of the two pKa values for all the PPIs. These values predict their relative acid stability and thus the rate of reaction with cysteines of the active proton pump at the pH of the secreting parietal cell. The PPI accumulates in the secretory canaliculus of the parietal cell due to pyridine protonation then binds to the pump and is activated by the second protonation on the surface of the protein to allow disulfide formation.

IT 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole**
117976-89-3, Rabeprazole
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemical of covalent inhibition of gastric (H+, K+)-ATPase by proton pump inhibitors)

L2 ANSWER 14 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:453207 CAPLUS
DOCUMENT NUMBER: 141:12318
TITLE: **Stable lansoprazole** containing more than 500-3000 ppm water and 200-5000 ppm alcohol
INVENTOR(S): Singer, Claude; Liberman, Anita; Veinberg, Irena
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004046135	A1	20040603	WO 2003-US37164		20031118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
EP 1465890	A1	20041013	EP 2003-789888		20031118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2004215021	A1	20041028	US 2003-717325		20031118
PRIORITY APPLN. INFO.:			US 2002-427589P	P	20021118
			US 2003-445219P	P	20030205
			WO 2003-US37164	W	20031118

AB The present invention provides a **stable lansoprazole** comprising either 500-3000 ppm water and 200-5000 ppm alc., or both. The present invention provides a method of preparing a **stable lansoprazole** as well as a pharmaceutical composition containing same. The present invention further provides a method of purifying **lansoprazole** that is substantially free of sulfone and sulfide derivs.

TI **Stable lansoprazole** containing more than 500-3000 ppm water and 200-5000 ppm alcohol

AB The present invention provides a **stable lansoprazole** comprising either 500-3000 ppm water and 200-5000 ppm alc., or both. The present invention provides a method of preparing a **stable lansoprazole** as well as a pharmaceutical composition containing same. The present invention further provides a method of purifying lansoprazole that is substantially free of sulfone and sulfide derivs.

ST lansoprazole compn **stable** water alc

IT Crystallization
Drug delivery systems
(**stable lansoprazole** containing more than 500-3000 ppm water and 200-5000 ppm alc.)

IT Drug delivery systems
(tablets; **stable lansoprazole** containing more than 500-3000 ppm water and 200-5000 ppm alc.)

IT 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(stable **lansoprazole** containing more than 500-3000 ppm water and 200-5000 ppm alc.)

IT 64-17-5, Ethanol, uses
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process); USES (Uses)
(**stable lansoprazole** containing more than 500-3000 ppm water and 200-5000 ppm alc.)

IT 103577-45-3, **Lansoprazole**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**stable lansoprazole** containing more than 500-3000 ppm water and 200-5000 ppm alc.)

IT 64-18-6, Formic acid, processes 64-19-7, Acetic acid, processes 67-56-1, Methanol, processes 67-63-0, 2-Propanol, processes 67-64-1, Acetone, processes 68-12-2, Dmf, processes 71-23-8, 1-Propanol, processes 74-89-5, Methylamine, processes 78-93-3, 2-Butanone, processes 102-71-6, Triethanolamine, processes 105-58-8, Diethyl carbonate 109-89-7, Diethylamine, processes 109-99-9, Thf, processes 111-42-2, Diethanolamine, processes 121-44-8, Triethylamine, processes 616-38-6, Dimethyl carbonate 1336-21-6, Ammonium hydroxide 7647-01-0, Hydrochloric acid, processes 7664-41-7, Ammonia, processes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(**stable lansoprazole** containing more than 500-3000 ppm water and 200-5000 ppm alc.)

L2 ANSWER 15 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:354792 CAPLUS
DOCUMENT NUMBER: 140:327137
TITLE: **Stable** solid preparations containing amorphous benzimidazoles and salts
INVENTOR(S): Nonomura, Muneo; Ito, Hiroki; Hashimoto, Hideo; Urai, Tadashi
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2004035052	A1	20040429	WO 2003-JP13152		20031015
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
JP 2004155773	A2	20040603	JP 2003-354904		20031015
PRIORITY APPLN. INFO.:			JP 2002-301893	A	20021016

OTHER SOURCE(S): MARPAT 140:327137

AB It is intended to provide a process for producing unstable amorphous benzimidazole compds. having a proton pump inhibitor function, and **stable** solid prepns. for medicinal use containing these compds. which are produced by blending such an amorphous benzimidazole compound with a nontoxic base such as a basic inorg. salt, forming an intermediate coating layer on the layer containing the active ingredient and further forming an enteric coating layer or a release-controlling coating layer. For example, granules were formulated containing amorphous (R)-**lansoprazole**, MgCO3, and excipients, treated with an enteric-soluble coating composition containing methacrylate copolymer, then filled into capsules.

REFERENCE COUNT: 164 THERE ARE 164 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI **Stable** solid preparations containing amorphous benzimidazoles and salts

AB It is intended to provide a process for producing unstable amorphous benzimidazole compds. having a proton pump inhibitor function, and stable solid prepns. for medicinal use containing these compds. which are produced by blending such an amorphous benzimidazole compound with a nontoxic base such as a basic inorg. salt, forming an intermediate coating layer on the layer containing the active ingredient and further forming an enteric coating layer or a release-controlling coating layer. For example, granules were formulated containing amorphous (R)-**lansoprazole**, MgCO3, and excipients, treated with an enteric-soluble coating composition containing methacrylate copolymer, then filled into capsules.

ST amorphous benzimidazole proton pump inhibitor salt granule stability; **lansoprazole** magnesium carbonate granule enteric coating capsule

IT Drug delivery systems
(capsules; **stable** solid prepns. containing amorphous benzimidazole proton pump inhibitors and salts)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proton pump, inhibitors; **stable** solid prepns. containing amorphous benzimidazole proton pump inhibitors and salts)

IT Drug delivery systems
(solids, enteric-coated; **stable** solid prepns. containing amorphous benzimidazole proton pump inhibitors and salts)

IT 313640-86-7
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** solid prepns. containing amorphous benzimidazole proton pump inhibitors and salts)

IT 144-55-8, Sodium hydrogen carbonate, biological studies 471-34-1, Calcium carbonate, biological studies 497-19-8, Sodium carbonate, biological studies 546-93-0, Magnesium carbonate 1309-42-8, Magnesium

hydroxide 1309-48-4, Magnesia, biological studies 1343-88-0, Magnesium silicate 7647-14-5, Sodium chloride, biological studies 12304-65-3, Hydrotalcite 21645-51-2, Aluminum hydroxide, biological studies 119141-88-7, S-Omeprazole 119141-89-8 138530-94-6 138530-95-7, S-**Lansoprazole** 142678-35-1, S-Pantoprazole 142706-18-1 177795-59-4, S-Rabeprazole 177795-60-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** solid prepns. containing amorphous benzimidazole proton pump inhibitors and salts)

L2 ANSWER 16 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:162580 CAPLUS
DOCUMENT NUMBER: 140:187434
TITLE: A process for manufacture of **stable** oral multiple unit pharmaceutical composition containing benzimidazoles
INVENTOR(S): Antarkar, Amit Krishna; Abdul Sattar Abdul, Javed; Lala Rajendra, Ghanshamlal; Joshi Ketaki, Kishore; Gadkari Parag, Narayan; Thanawala Gaurang, Hasmukhlal; Shah Maya, Janak; Shah Janak, Ramanlal
PATENT ASSIGNEE(S): Themis Laboratories Private Limited, India
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004016242	A2	20040226	WO 2003-IB3514	20030804
WO 2004016242	A3	20040408		
WO 2004016242	C1	20041007		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1530460	A2	20050518	EP 2003-787961	20030804
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: IN 2002-MU742 A 20020816
WO 2003-IB3514 W 20030804

AB This invention relates to process for manufacture of a **stable**, oral, multiple unit pharmaceutical composition containing high concentration of benzimidazole up to 40% by weight without the use of micronized benzimidazole, disintegrating agent and fillers. Surfactants in these compns. are in enteric polymer layer and not in contact with benzimidazole. Multiple unit pharmaceutical composition of the invention shows min. acid degradation in 0.1 N HCl after 2 h and pH 6.8 buffer release of more than 85% after 45 min. The multiple unit pharmaceutical composition is in the form unagglomerated, uniformly shaped and sized enteric-coated pellets, which are processed continuously or in batches in single equipment such as fluid bed bottom spray processor. The invention involves sequential deposition of alkaline material layer on non-pareil seeds to obtain treated non-pareil seeds, drug layer to obtain

drug pellets, sealant polymer layer to obtain sealed pellets, and enteric polymer layer to obtain enteric coated pellets. The enteric-coated pellets obtained are capable of being filled in smallest size capsules for ease of administration and patient acceptance. Enteric-coated pellets contained omeprazole 24.5, non-pareil seeds 32.3, HPMC-E15 7.3, NaOH 3.2, talc 3.7, and water qs to 100%.

TI A process for manufacture of **stable** oral multiple unit pharmaceutical composition containing benzimidazoles

AB This invention relates to process for manufacture of a **stable**, oral, multiple unit pharmaceutical composition containing high concentration of benzimidazole up to 40% by weight without the use of micronized benzimidazole, disintegrating agent and fillers. Surfactants in these compns. are in enteric polymer layer and not in contact with benzimidazole. Multiple unit pharmaceutical composition of the invention shows min. acid degradation in 0.1 N HCl after 2 h and pH 6.8 buffer release of more than 85% after 45 min. The multiple unit pharmaceutical composition is in the form unagglomerated, uniformly shaped and sized enteric-coated pellets, which are processed continuously or in batches in single equipment such as fluid bed bottom spray processor. The invention involves sequential deposition of alkaline material layer on non-pareil seeds to obtain treated non-pareil seeds, drug layer to obtain drug pellets, sealant polymer layer to obtain sealed pellets, and enteric polymer layer to obtain enteric coated pellets. The enteric-coated pellets obtained are capable of being filled in smallest size capsules for ease of administration and patient acceptance. Enteric-coated pellets contained omeprazole 24.5, non-pareil seeds 32.3, HPMC-E15 7.3, NaOH 3.2, talc 3.7, and water qs to 100%.

IT Drug delivery systems
(capsules; manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)

IT Binders
Dissolution
Drug bioavailability
Drug bioequivalence
Fillers
Human
Plasticizers
Surfactants
(manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)

IT Alkali metal hydroxides
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)

IT Drug delivery systems
(oral; manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)

IT Drug delivery systems
(pellets, enteric-coated; manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)

IT Drug delivery systems
(tablets, enteric-coated; manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)

IT 1305-62-0, Calcium hydroxide, processes 1309-42-8, Magnesium hydroxide 1310-58-3, Potassium hydroxide, processes 1310-73-2, Sodium hydroxide, processes 1336-21-6, Ammonium hydroxide

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)

IT 51-17-2D, Benzimidazole, derivs. 73590-58-6, Omeprazole 103577-45-3, **Lansoprazole**
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)

IT 79-41-4D, Methacrylic acid, polymers 546-93-0, Magnesium carbonate 7631-86-9, Silicon dioxide, biological studies 9003-39-8, Polyvinylpyrrolidone 9004-32-4, Sodium carboxymethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9004-67-5, Methyl cellulose 14807-96-6, Talc, biological studies 18641-57-1, Glyceryl behenate 31566-31-1, Glyceryl monostearate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)

L2 ANSWER 17 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:119766 CAPLUS
DOCUMENT NUMBER: 140:152014
TITLE: Enteric coated oral pharmaceutical compositions of acid-unstable drugs
INVENTOR(S): Deshpande, Jayant Venkatesh; Gupte, Vandana Sandeep; Kadam, Vaishali Madhukar; Gosar, Chandrakant Thakarsi; Deshmukh, Satish Ramachandra; Gupte, Rajan Vitthal; Tamhankar, Vijay Ramachandra
PATENT ASSIGNEE(S): Kopran Research Laboratories Limited, India
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004028737	A1	20040212	US 2002-216315	20020812

PRIORITY APPLN. INFO.: US 2002-216315 20020812

AB Enteric coated **stable** oral pharmaceutical compns. of acid-unstable drugs are described. The enteric coating is a bilayer with a pH gradient across its thickness comprising an inner layer of neutral or near neutral pH 7-7.5 and an outer layer of acidic pH 2-6. The enteric coating is first carried out at neutral or near neutral pH of 7-7.5 to form an inner layer of neutral or near neutral pH and then at acidic pH of 2-6 to form an outer layer of acidic pH. Tablets of the following composition were prepared: omeprazole 10.30, anhydrous lactose 55.00, Mg stearate 1.00, talc 1.00, colloidal silicon dioxide 0.50, microcryst. cellulose 17.00, corn starch 10.00, and Povidone 3.00 mg. The tablets were enteric coated with the following aqueous organic dispersion of enteric coating material at neutral pH 7: methacrylate copolymer type C 0.4, PEG-600 0.04, Polysorbate-80 0.02, titanium dioxide 0.05, and talc 0.165 kg, iso-Pr alc. 4.0 and Water 0.375 L.

AB Enteric coated **stable** oral pharmaceutical compns. of acid-unstable drugs are described. The enteric coating is a bilayer with a pH gradient across its thickness comprising an inner layer of neutral or near neutral pH 7-7.5 and an outer layer of acidic pH 2-6. The enteric coating is first carried out at neutral or near neutral pH of 7-7.5 to form an inner layer of neutral or near neutral pH and then at acidic pH of

2-6 to form an outer layer of acidic pH. Tablets of the following composition were prepared: omeprazole 10.30, anhydrous lactose 55.00, Mg stearate 1.00, talc 1.00, colloidal silicon dioxide 0.50, microcryst. cellulose 17.00, corn starch 10.00, and Povidone 3.00 mg. The tablets were enteric coated with the following aqueous organic dispersion of enteric coating material at neutral pH 7: methacrylate copolymer type C 0.4, PEG-600 0.04, Polysorbate-80 0.02, titanium dioxide 0.05, and talc 0.165 kg, iso-Pr alc. 4.0 and Water 0.375 L.

IT 51-17-2D, Benzimidazole, derivs. 59-92-7, Levodopa, biological studies 61-32-5, Methicillin 79-41-4D, Methacrylic acid, esters, polymers 114-07-8, Erythromycin 1406-05-9, Penicillin 4697-36-3, Carbenicillin 8049-47-6, Pancreatin 9004-10-8, Insulin, biological studies 20830-75-5, Digoxin 65277-42-1, Ketoconazole 69655-05-6, Didanosine 73590-58-6, Omeprazole 81093-37-0, Pravastatin 84625-61-6, Itraconazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 117976-89-3, Rabeprazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteric coated oral pharmaceutical compns. of acid-unstable drugs)

L2 ANSWER 18 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:60341 CAPLUS
DOCUMENT NUMBER: 140:117406
TITLE: Liquid dosage compositions of **stable** nanoparticulate drugs
INVENTOR(S): Bosch, William H.; Hilborn, Matthew R.; Hovey, Douglas C.; Kline, Laura J.; Lee, Robert W.; Pruitt, John D.; Ryde, Niels P.; Ryde, Tuula A.; Xu, Shuqian
PATENT ASSIGNEE(S): Elan Pharma International, Ltd, Ire.
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004006959	A1	20040122	WO 2003-US22187		20030716
WO 2004006959	C1	20050331			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2492488	AA	20040122	CA 2003-2492488		20030716
PRIORITY APPLN. INFO.:			US 2002-396530P	P	20020716
			WO 2003-US22187	W	20030716

AB The present invention relates to liquid dosage compns. of **stable** nanoparticulate drugs. The liquid dosage compns. of the invention include osmotically active crystal growth inhibitors that stabilize the nanoparticulate active agents against crystal and particle size growth of the drug. Thus, an aqueous nanoparticulate colloidal dispersion (NCD) comprising drug 32.5 Copovidone 6.5, and dioctyl sodium sulfosuccinate 0.464% by weight was prepared by milling for 3.8 h under high energy milling conditions. The final mean particle size (by weight) of the drug particles was 161 nm. The concentrated NCD was then diluted with preserved water and glycerol (the osmotically active crystal growth inhibitor) to 0.5-3.0%

drug.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Liquid dosage compositions of **stable** nanoparticulate drugs
AB The present invention relates to liquid dosage compns. of **stable** nanoparticulate drugs. The liquid dosage compns. of the invention include osmotically active crystal growth inhibitors that stabilize the nanoparticulate active agents against crystal and particle size growth of the drug. Thus, an aqueous nanoparticulate colloidal dispersion (NCD) comprising drug 32.5 Copovidone 6.5, and dioctyl sodium sulfosuccinate 0.464% by weight was prepared by milling for 3.8 h under high energy milling conditions. The final mean particle size (by weight) of the drug particles was 161 nm. The concentrated NCD was then diluted with preserved water and glycerol (the osmotically active crystal growth inhibitor) to 0.5-3.0% drug.
ST liq dosage **stable** nanoparticulate drug
IT Inflammation
(Crohn's disease; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Intestine, disease
(Crohn's; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Alcohols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C16-18, ethoxylated; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Alcohols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C16-18; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Arthritis
(Reiter's syndrome; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(aerosols; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Diagnosis
(agents; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkyl group-terminated; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkylbenzyldimethyl, chlorides; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkyltrimethyl, chlorides; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkyltrimethyl, ethoxylated; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Fats and Glyceridic oils, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(animal, marine; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Inflammation
Spinal column, disease
(ankylosing spondylitis; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Polyethers, biological studies

138402-11-6, Irbesartan 139481-59-7, Candesartan 139755-83-2, Sildenafil 144034-80-0, Rizatriptan 145599-86-6, Cerivastatin 147059-72-1, Trovafloxacin 159989-65-8, Nelfinavir mesylate 283158-20-3 329326-68-3, p-Isononylphenoxypolyglycidol 503178-50-5 608094-65-1, PEG-vitamin A 630400-66-7 630400-67-8 634601-99-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)

L2 ANSWER 19 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:41242 CAPLUS
DOCUMENT NUMBER: 140:82283
TITLE: Long-term **stable** oral pharmaceutical formulation of microgranules in suspension
INVENTOR(S): Artalejo Ortega, Beatriz; Batllori Calbo, Javier; Fernandez Garcia, Andres; Julve Rubio, Jordi
PATENT ASSIGNEE(S): Laboratorios S.A.L.V.A.T., S.A., Spain
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004682	A2	20040115	WO 2003-EP6927	20030630
WO 2004004682	A3	20041028		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: ES 2002-1610 A 20020702

AB Disclosed are pharmaceutical formulations obtained by subjecting conventional microgranules to an external seal-coating layer that avoids the penetration of liquid vehicle, and selecting a hydrophobic liquid vehicle with a viscosity high enough not to wet the microgranules. The seal-coating layer may be obtained by coating the microgranules with an aqueous suspension comprising film formers and plasticizers. The liquid vehicle is comprised of oily solvents and viscosity agents. The formulation is presented in single dose sachets ready-to-use. This formulation enables the liquid oral administration of antiulcerous microgranules of benzimidazoles, preferably **lansoprazole**, with several advantages comparing to com. available suspensions. The new formulation of **lansoprazole** microgranules has a similar bioavailability and slightly higher stability than conventional hard gelatin capsules. For example, conventional microgranules of **lansoprazole** were subjected to an addnl. seal coating with a composition containing hydroxypropyl Me cellulose 10, polyethylene glycol 5, and purified water q.s. to 100 %. The coated granules were suspended in an oily vehicle containing lauroyl macrogol-32 glyceride 4, ammonium glycyrrhizinate 0.5, Na saccharin 0.1, Na cyclamate 2, flavoring 1, and medium-chain glycerides balance to 100 %. The oily suspension obtained were packaged in single-dose sachets.

TI Long-term **stable** oral pharmaceutical formulation of microgranules in suspension

AB Disclosed are pharmaceutical formulations obtained by subjecting conventional microgranules to an external seal-coating layer that avoids the penetration of liquid vehicle, and selecting a hydrophobic liquid vehicle with a viscosity high enough not to wet the microgranules. The seal-coating layer may be obtained by coating the microgranules with an aqueous suspension comprising film formers and plasticizers. The liquid vehicle is comprised of oily solvents and viscosity agents. The formulation is presented in single dose sachets ready-to-use. This formulation enables the liquid oral administration of antiulcerous microgranules of benzimidazoles, preferably **lansoprazole**, with several advantages comparing to com. available suspensions. The new formulation of lansoprazole microgranules has a similar bioavailability and slightly higher stability than conventional hard gelatin capsules. For example, conventional microgranules of **lansoprazole** were subjected to an addnl. seal coating with a composition containing hydroxypropyl Me cellulose 10, polyethylene glycol 5, and purified water q.s. to 100 %. The coated granules were suspended in an oily vehicle containing lauroyl macrogol-32 glyceride 4, ammonium glycyrrhizinate 0.5, Na saccharin 0.1, Na cyclamate 2, flavoring 1, and medium-chain glycerides balance to 100 %. The oily suspension obtained were packaged in single-dose sachets.

ST antiulcer granule oral suspension bioavailability; **lansoprazole** granule cellulose ether coating suspension

IT Glycerides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medium-chain; seal-coated microgranules in liquid vehicles for manufacturing **stable** oral suspensions)

IT Antiulcer agents
Drug bioavailability
(seal-coated microgranules in liquid vehicles for manufacturing **stable** oral suspensions)

IT Corn oil
Lecithins
Peanut oil
Polyoxyalkylenes, biological studies
Soybean oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(seal-coated microgranules in liquid vehicles for manufacturing **stable** oral suspensions)

IT Glycerides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(short-chain; seal-coated microgranules in liquid vehicles for manufacturing stable oral suspensions)

IT Drug delivery systems
(suspensions, oral; seal-coated microgranules in liquid vehicles for manufacturing **stable** oral suspensions)

IT 7631-86-9, Silica, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(colloidal; seal-coated microgranules in liquid vehicles for manufacturing **stable** oral suspensions)

IT 77-93-0, Triethyl citrate 88-99-3D, Phthalic acid, esters 109-43-3, Dibutyl decanedioate 112-92-5, Stearyl alcohol 9003-39-8, PVP 9004-65-3, Hydroxypropyl methyl cellulose 9005-32-7, Alginic acid 11138-66-2, Xanthan gum 24938-16-7, Eudragit EPO 25322-68-3, Polyethylene glycol 26942-95-0, Triisostearin 31566-31-1, Glyceryl monostearate 36653-82-4, Cetyl alcohol 103577-45-3, **Lansoprazole**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(seal-coated microgranules in liquid vehicles for manufacturing **stable** oral suspensions)

L2 ANSWER 20 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:605606 CAPLUS
DOCUMENT NUMBER: 140:263770
TITLE: Assessment of potential digoxin-rabeprazole interaction after formulary conversion of proton-pump inhibitors
AUTHOR(S): Le, Grace H.; Schaefer, Monica G.; Plowman, Brian K.; Morreale, Anthony P.; Delattre, Melissa; Okino, Lisa; Felicio, Leda
CORPORATE SOURCE: Veterans Affairs San Diego Healthcare System (VASDHS), San Diego, CA, USA
SOURCE: American Journal of Health-System Pharmacy (2003), 60(13), 1343-1345
CODEN: AHSPEK; ISSN: 1079-2082
PUBLISHER: American Society of Health-System Pharmacists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A nonblinded, nonrandomized, prospective, observational drug utilization evaluation was carried out to assess the digoxin levels before and after the conversion to rabeprazole to ensure the it would not neg. affect digoxin levels and treatment outcomes. The mean ± standard deviation serum digoxin concentration did not change significantly in patients whose proton-pump inhibitor therapy was changed from **lansoprazole** or omeprazole to rabeprazole. The greater than 15% increase in digoxin levels that occurred in 12 patients could have been clin. significant had they had serum digoxin levels at or near the upper limit of the therapeutic range when rabeprazole was added. This suggests that it is necessary to establish a baseline digoxin level and monitor for adverse effects during a conversion of **stable** digoxin recipients from one proton-pump inhibitor to another.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB A nonblinded, nonrandomized, prospective, observational drug utilization evaluation was carried out to assess the digoxin levels before and after the conversion to rabeprazole to ensure the it would not neg. affect digoxin levels and treatment outcomes. The mean ± standard deviation serum digoxin concentration did not change significantly in patients whose proton-pump inhibitor therapy was changed from **lansoprazole** or omeprazole to rabeprazole. The greater than 15% increase in digoxin levels that occurred in 12 patients could have been clin. significant had they had serum digoxin levels at or near the upper limit of the therapeutic range when rabeprazole was added. This suggests that it is necessary to establish a baseline digoxin level and monitor for adverse effects during a conversion of **stable** digoxin recipients from one proton-pump inhibitor to another.
IT Human
(assessment of potential digoxin-rabeprazole interaction after formulary conversion of proton-pump inhibitors from **lansoprazole** or omeprazole to rabeprazole)
IT Drug interactions
(pharmacokinetic; assessment of potential digoxin-rabeprazole interaction after formulary conversion of proton-pump inhibitors from **lansoprazole** or omeprazole to rabeprazole)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proton pump; assessment of potential digoxin-rabeprazole interaction after formulary conversion of proton-pump inhibitors from **lansoprazole** or omeprazole to rabeprazole)
IT 117976-89-3, Rabeprazole

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(assessment of potential digoxin-rabeprazole interaction after formulary conversion of proton-pump inhibitors from **lansoprazole** or omeprazole to rabeprazole)

IT 20830-75-5, Digoxin
RL: ADV (Adverse effect, including toxicity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(assessment of potential digoxin-rabeprazole interaction after formulary conversion of proton-pump inhibitors from **lansoprazole** or omeprazole to rabeprazole)

IT 73590-58-6, Omeprazole 103577-45-3, **Lansoprazole**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(assessment of potential digoxin-rabeprazole interaction after formulary conversion of proton-pump inhibitors from **lansoprazole** or omeprazole to rabeprazole)

L2 ANSWER 21 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:242161 CAPLUS
DOCUMENT NUMBER: 138:260473
TITLE: Pharmaceutical formulations for protecting pharmaceutical compound from acidic environments
INVENTOR(S): Taneja, Rajneesh; Gupta, Pramrod
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024449	A1	20030327	WO 2002-US22229	20020712
W: CA, JP, MX				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
US 2003235628	A1	20031225	US 2001-955801	20010919
CA 2460987	AA	20030327	CA 2002-2460987	20020712
EP 1429766	A1	20040623	EP 2002-750005	20020712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR, BG, CZ, EE, SK				
JP 2005507883	T2	20050324	JP 2003-528545	20020712
PRIORITY APPLN. INFO.:			US 2001-955801 A	20010919
			WO 2002-US22229 W	20020712

AB Pharmaceutical compns. for protecting acid-labile drugs, such as a proton pump inhibitor, in acidic environment comprise a protectant, i.e., a water-soluble or water-insol. acid neutralizer. For example, granules were prepared containing **lansoprazole** 30 mg, magnesium hydroxide 350 mg, calcium carbonate 140 mg, sucrose 120 mg, and tromethamine 350 mg. **Lansoprazole** was **stable** in the granules kept in a closed container at room temperature for 27 days.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Pharmaceutical compns. for protecting acid-labile drugs, such as a proton pump inhibitor, in acidic environment comprise a protectant, i.e., a water-soluble or water-insol. acid neutralizer. For example, granules were prepared containing **lansoprazole** 30 mg, magnesium hydroxide 350 mg, calcium carbonate 140 mg, sucrose 120 mg, and tromethamine 350 mg. **Lansoprazole** was **stable** in the granules kept in a closed container at room temperature for 27 days.

IT 103577-45-3, **Lansoprazole**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acid neutralizers for protecting acid-labile drugs in acidic environment)

L2 ANSWER 22 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:173403 CAPLUS
DOCUMENT NUMBER: 138:210335
TITLE: **Stable** pharmaceutical compositions comprising acid labile benzimidazoles
INVENTOR(S): Sugaya, Masae; Shimizu, Toshihiro
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003017980	A1	20030306	WO 2002-JP8704	20020829
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2448760	AA	20030306	CA 2002-2448760	20020829
JP 2003327533	A2	20031119	JP 2002-251254	20020829
EP 1420763	A1	20040526	EP 2002-765367	20020829
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004248939	A1	20041209	US 2004-487809	20040226

PRIORITY APPLN. INFO.:

JP 2001-263481	A	20010831
JP 2001-341477	A	20011107
JP 2002-60006	A	20020306
WO 2002-JP8704	W	20020829

OTHER SOURCE(S): MARPAT 138:210335

AB A solid composition, without enteric coating, contains an acid-labile active ingredient, particularly, a benzimidazole having an antiulcer activity. This composition neutralizes the acid in the stomach quickly, exerts quickly the pharmacol. effect of the drug and suppresses the formation of CO2. A gastric disintegrable solid composition contains in addition to the drug at least 1 component selected from metal oxides and metal hydroxides. The composition has a disintegration time of ≤7 min. **Lansoprazole** 240 g, 1160 g Mg(OH)2, 616 g D-mannitol, and 264 g corn starch were charged into a fluidized-bed granulator, and 8% aqueous solution prepared by dissolving 120 g of hydroxypropyl cellulose in 1380 g water was sprayed, and these materials were granulated, and dried to obtain 2188 g of granules (active ingredient group). Mg(OH)2 870 g, 1107 g of D-mannitol and 474 g of corn starch were charged in a fluidized bed granulator, and 750 g water was sprayed, and these materials were granulated, and dried to obtain 2199 g of granules (outer layer group). The active ingredient group 300 g, 408.5 g the outer

layer group, 37.5 g Crospovidone and 11 g Mg stearate were mixed in a bag to obtain a mixture The resultant mixture was compressed into tablets (750 mg/tablet). No darkishness by whittled powders or sticking of the mixture on the die was observed in the resulting tablets.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI **Stable** pharmaceutical compositions comprising acid labile benzimidazoles

AB A solid composition, without enteric coating, contains an acid-labile active ingredient, particularly, a benzimidazole having an antiulcer activity. This composition neutralizes the acid in the stomach quickly, exerts quickly the pharmacol. effect of the drug and suppresses the formation of CO2. A gastric disintegrable solid composition contains in addition to the drug at least 1 component selected from metal oxides and metal hydroxides. The composition has a disintegration time of ≤7 min. **Lansoprazole** 240 g, 1160 g Mg(OH)2, 616 g D-mannitol, and 264 g corn starch were charged into a fluidized-bed granulator, and 8% aqueous solution prepared by dissolving 120 g of hydroxypropyl cellulose in 1380 g water was sprayed, and these materials were granulated, and dried to obtain 2188 g of granules (active ingredient group). Mg(OH)2 870 g, 1107 g of D-mannitol and 474 g of corn starch were charged in a fluidized bed granulator, and 750 g water was sprayed, and these materials were granulated, and dried to obtain 2199 g of granules (outer layer group). The active ingredient group 300 g, 408.5 g the outer layer group, 37.5 g Crospovidone and 11 g Mg stearate were mixed in a bag to obtain a mixture The resultant mixture was compressed into tablets (750 mg/tablet). No darkishness by whittled powders or sticking of the mixture on the die was observed in the resulting tablets.

IT Carbonates, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkaline earth; **stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT Drug delivery systems
(capsules; **stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT Drug delivery systems
(granules; **stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proton pump, inhibitors; **stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT Calcination
Surface area
(**stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT Hydroxides (inorganic)
Oxides (inorganic), biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT Drug delivery systems
(tablets; **stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT 21645-51-2, Aluminum hydroxide (Al(OH)3), biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gels; **stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT 1309-48-4, Magnesium oxide (MgO), biological studies
RL: FMU (Formation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES

(Uses)
(**stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT 74-79-3, L-Arginine, biological studies 77-86-1, Trometamol 150-90-3, Disodium succinate 7558-79-4, DiSodium phosphate 7601-54-9, TriSodium phosphate
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT 144-55-8, Carbonic acid monosodium salt, biological studies 471-34-1, Calcium carbonate, biological studies 546-93-0, Magnesium carbonate 1343-88-0, Magnesium silicate 12304-65-3, Hydrotalcite 12511-31-8 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, Lansoprazole 117976-89-3, Rabeprazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

L2 ANSWER 23 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:958602 CAPLUS
DOCUMENT NUMBER: 138:29133
TITLE: Formulation of **stable** antiulcer oral preparations
INVENTOR(S): Machiba, Yasuo; Ikemoto, Keiichi; Tatsumi, Asaki; Asada, Kazuyoshi
PATENT ASSIGNEE(S): Towa Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002363080	A2	20021218	JP 2001-173557	20010608

PRIORITY APPLN. INFO.: JP 2001-173557 20010608

AB **Stable** antiulcer oral prepns., including enteric coated tablets, containing omeprazole, **lansoprazole**, and rabeprazole, and their alkali salts, are formulated by granulating and coating with film-forming water-soluble polymers and tableting with dispersing agents, etc.

TI Formulation of **stable** antiulcer oral preparations

AB Stable antiulcer oral prepns., including enteric coated tablets, containing omeprazole, **lansoprazole**, and rabeprazole, and their alkali salts, are formulated by granulating and coating with film-forming water-soluble polymers and tableting with dispersing agents, etc.

IT Antiulcer agents
Dispersing agents
Stability
(formulation of **stable** antiulcer oral prepns.)

IT Polymers, biological studies
Polyoxyalkylenes, biological studies
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulation of **stable** antiulcer oral prepns.)

IT Drug delivery systems
(oral; formulation of **stable** antiulcer oral prepns.)

IT Drug delivery systems
(tablets, enteric-coated; formulation of **stable** antiulcer oral prepns.)

IT 9004-64-2, Hydroxypropylcellulose 25322-68-3, PEG 6000 73590-58-6,

Omeprazole 103577-45-3, **Lansoprazole** 117976-89-3, Rabeprazole
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulation of **stable** antiulcer oral prepns.)

L2 ANSWER 24 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:636460 CAPLUS
DOCUMENT NUMBER: 137:159367
TITLE: Enteric coated preparations containing proton pump inhibitors
INVENTOR(S): Hirata, Kenji; Mori, Masaki
PATENT ASSIGNEE(S): Kyowa Yakuhin Kogyo K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002234842	A2	20020823	JP 2001-77232	20010209
US 2004146558	A1	20040729	US 2003-352141	20030128

PRIORITY APPLN. INFO.: JP 2001-77232 A 20010209

AB This invention relates to **stable** enteric-soluble compns. which contain benzimidazole-type proton pump inhibitors. The compns. show little variation in drug release onset time. The compns. comprise (1) a core containing benzimidazoles as active ingredients and alkalies, (2) a water-insol. membrane coating containing dispersed water-soluble substance particles, and (3) an enteric-soluble coating. An enteric-coated tablet was formulated containing omeprazole 20, lactose 70, starch 21, low-substituted hydroxypropyl cellulose 6, hydroxypropyl cellulose 1, talc 2, and Mg stearate 1 mg.

AB This invention relates to **stable** enteric-soluble compns. which contain benzimidazole-type proton pump inhibitors. The compns. show little variation in drug release onset time. The compns. comprise (1) a core containing benzimidazoles as active ingredients and alkalies, (2) a water-insol. membrane coating containing dispersed water-soluble substance particles, and (3) an enteric-soluble coating. An enteric-coated tablet was formulated containing omeprazole 20, lactose 70, starch 21, low-substituted hydroxypropyl cellulose 6, hydroxypropyl cellulose 1, talc 2, and Mg stearate 1 mg.

IT 57-50-1, White sugar, biological studies 63-42-3, Lactose 69-65-8, D-Mannitol 99-20-7, Trehalose 144-55-8, Sodium hydrogen carbonate, biological studies 497-19-8, Sodium carbonate, biological studies 7632-05-5, Sodium phosphate 9004-38-0, Cellulose acetate phthalate 9004-57-3, Ethyl cellulose 9005-25-8, Starch, biological studies 9050-31-1, Hydroxypropyl methyl cellulose phthalate 25086-15-1, Methacrylic acidmethyl methacrylate copolymer 37205-99-5, Carboxymethyl ethyl cellulose 53237-50-6 71138-97-1, Hydroxypropyl methyl cellulose acetate succinate 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 117976-89-3, Rabeprazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteric coated prepns. containing proton pump inhibitors)

L2 ANSWER 25 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:555334 CAPLUS
DOCUMENT NUMBER: 137:114525
TITLE: Syntactic deformable pharmaceutical foam compositions
INVENTOR(S): Odidi, Isa; Odidi, Amina
PATENT ASSIGNEE(S): Can.

SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002056861	A2	20020725	WO 2002-CA54	20020117
WO 2002056861	A3	20021017		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 6800668	B1	20041005	US 2001-765783	20010119
CA 2435276	AA	20020725	CA 2002-2435276	20020117
CA 2435276	C	20050315		

PRIORITY APPLN. INFO.: US 2001-765783 A 20010119
WO 2002-CA54 W 20020117

AB The invention relates to methods for preparing a syntactic foam composition suitable for use as a carrier for chems. or other compds., including pharmaceuticals. Carbopol 971P, hydroxyethyl cellulose, cellulose microspheres and silica, was mixed in a high-shear mixer. The resulting admixt. was treated with 2-propanol, while simultaneously subjecting the admixt. to high-shear forces in the high-shear mixer. This mixing created a uniform **stable** syntactic deformable and compressible dendritic solid foam which could be shaped before drying. Metoprolol succinate was added to the above admixt. and subjected to high-shear agitation for 2 min before treatment with 2-propanol. A **stable** syntactic deformable and compressible dendritic solid foam which could be shaped before drying was obtained. This was dried at 40°. The dried foam was the disentangled by size reduction to obtain discrete particles. The free flowing particles were reassembled and shaped by compression in a mold. The shaped units, when subjected to an aqueous medium, released metoprolol over a period of ≤3 h.

AB The invention relates to methods for preparing a syntactic foam composition suitable for use as a carrier for chems. or other compds., including pharmaceuticals. Carbopol 971P, hydroxyethyl cellulose, cellulose microspheres and silica, was mixed in a high-shear mixer. The resulting admixt. was treated with 2-propanol, while simultaneously subjecting the admixt. to high-shear forces in the high-shear mixer. This mixing created a uniform **stable** syntactic deformable and compressible dendritic solid foam which could be shaped before drying. Metoprolol succinate was added to the above admixt. and subjected to high-shear agitation for 2 min before treatment with 2-propanol. A **stable** syntactic deformable and compressible dendritic solid foam which could be shaped before drying was obtained. This was dried at 40°. The dried foam was the disentangled by size reduction to obtain discrete particles. The free flowing particles were reassembled and shaped by compression in a mold. The shaped units, when subjected to an aqueous medium, released metoprolol over a period of ≤3 h.

IT 50-02-2, Dexamethasone 50-28-2, Estradiol, biological studies 50-48-6, Amitriptyline 50-70-4, Sorbitol, biological studies 50-78-2, Aspirin 50-99-7, Glucose, biological studies 51-48-9, Levothyroxine, biological studies 53-03-2, Prednisone 54-31-9, Furosemide 57-27-2, Morphine,

biological studies 57-41-0, Phenytoin 57-50-1, Sucrose, biological studies 57-63-6, EthinylEstradiol 58-93-5, Hydrochlorothiazide 59-92-7, Levodopa, biological studies 60-87-7, Promethazine 63-42-3, Lactose 67-20-9, Nitrofurantoin 68-22-4, Norethindrone 69-65-8, Mannitol 76-42-6, Oxycodone 76-57-3, Codeine 78-44-4, Carisoprodol 81-81-2, Warfarin 83-43-2, Methylprednisolone 87-99-0, Xylitol 89-57-6, Mesalamine 90-82-4, Pseudoephedrine 93-14-1, Guaifenesin 99-66-1, Pentanoic acid, 2-propyl 103-90-2, Acetaminophen 114-07-8, Erythromycin 125-29-1, Hydrocodone 127-07-1, Hydroxyurea 132-98-9, Penicillin VK 155-09-9, Tranylcypromine 300-62-9D, Amphetamine, salts 303-53-7, Cyclobenzaprine 315-30-0, Allopurinol 378-44-9, Betamethasone 396-01-0, Triamterene 439-14-5, Diazepam 469-62-5, Propoxyphene 525-66-6, Propranolol 673-06-3, D-Phenylalanine 797-63-7, Levonorgestrel 846-49-1, Lorazepam 846-50-4, Temazepam 1119-34-2, L-Arginine hydrochloride 1622-61-3, Clonazepam 3056-17-5, Stavudine 3930-20-9, Sotalol 4205-90-7, Clonidine 4419-39-0, Beclomethasone 7447-40-7, Potassium Chloride, biological studies 7460-12-0, Pseudoephedrine sulfate 7481-89-2, Zalcitabine 7631-86-9, Silica, biological studies 9002-89-5, Polyvinyl alcohol 9002-96-4, α-Tocopherol polyethylene glycol succinate 9003-39-8, Povidone 9004-34-6, Cellulose, biological studies 9004-54-0, Dextran, biological studies 9004-62-0, Hydroxyethyl Cellulose 9004-65-3, Hydroxypropyl Methyl cellulose 9005-25-8, Starch, biological studies 9007-12-9, Calcitonin 10238-21-8, Glyburide 10540-29-1, Tamoxifen 11138-66-2, Xanthan gum 12650-69-0, Mupirocin 15686-71-2, Cephalexin 15687-27-1, Ibuprofen 16051-77-7, Isosorbide Mononitrate 18559-94-9, Albuterol 18641-57-1, Glyceryl behenate 19794-93-5, Trazodone 20830-75-5, Digoxin 21256-18-8, Oxaprozin 22204-53-1, Naproxen 23593-75-1, Clotrimazole 24980-41-4, Poly(ε-caprolactone) 25086-15-1, Eudragit L100 25248-42-4, Poly[oxy(1-oxo-1,6-hexanediyl)] 25322-68-3, Polyethylene glycol 25812-30-0, Gemfibrozil 26009-03-0, Poly(glycolic acid) 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(lactic acid) 26124-68-5, Poly(glycolic acid) 26787-78-0, Amoxicillin 28860-95-9, Carbidopa 28981-97-7, Alprazolam 29122-68-7, Atenolol 30516-87-1, Zidovudine 32986-56-4, Tobramycin 34346-01-5, Glycolic acid-lactic acid copolymer 51384-51-1, Metoprolol 54739-18-3, Fluvoxamine 54910-89-3, Fluoxetine 55268-75-2, Cefuroxime 56180-94-0, Acarbose 58001-44-8 59122-46-2, Misoprostol 59729-33-8, Citalopram 59803-98-4, Brimonidine 60205-81-4, Ipratropium 61869-08-7, Paroxetine 63590-64-7, Terazosin 63675-72-9, Nisoldipine 66357-35-5, Ranitidine 66376-36-1, Alendronate 66722-44-9, Bisoprolol 69655-05-6, Didanosine 72432-03-2, Miglitol 72509-76-3, Felodipine 72956-09-3, Carvedilol 74191-85-8, Doxazosin 75330-75-5, Lovastatin 75847-73-3, Enalapril 76547-98-3, Lisinopril 76584-70-8, Divalproex sodium 76824-35-6, Famotidine 76963-41-2, Nizatidine 78644-42-5, Poly(malic acid) 78666-19-0, Poly(malic acid), SRU 79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin 80474-14-2, Fluticasone Propionate 81093-37-0, Pravastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin 82419-36-1, Ofloxacin 82626-48-0, Zolpidem 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83905-01-5, Azithromycin 84449-90-1, Raloxifene 85441-61-8, Quinapril 85721-33-1, Ciprofloxacin 86541-75-5, Benazepril 87333-19-5, Ramipril 88150-42-9, Amlodipine 89365-50-4, Salmeterol 91161-71-6, Terbinafine 92665-29-7, Cefprozil 93413-69-5, Venlafaxine 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 97322-87-7, Troglitazone 98048-97-6, Fosinopril 98418-47-4, Metoprolol succinate 99614-02-5, Ondansetron 100986-85-4, Levofloxacin 103577-45-3, **Lansoprazole** 103628-46-2, Sumatriptan 104632-26-0, Pramipexole 105102-22-5, Mometasone 106133-20-4, Tamsulosin 106266-06-2, Risperidone 107753-78-6, Zafirlukast 109889-09-0, Granisetron 111974-69-7, Quetiapine 113665-84-2, Clopidogrel 114798-26-4, Losartan 120014-06-4, Donepezil 124937-51-5, Tolterodine 127779-20-8,

Saquinavir 129618-40-2, Nevirapine 130209-82-4, Latanoprost 132539-06-1, Olanzapine 134523-00-5, Atorvastatin 134678-17-4, Lamivudine 135062-02-1, Repaglinide 136470-78-5, Abacavir 136817-59-9, Delavirdine 137862-53-4, Valsartan 138402-11-6, Irbesartan 139755-83-2, Sildenafil 150378-17-9, Indinavir 151687-96-6, Carbopol 974P 154598-52-4, Efavirenz 155213-67-5, Ritonavir 158966-92-8, Montelukast 159989-64-7, Nelfinavir 161279-68-1, Carbopol 971P 161814-49-9, Amprenavir 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 192725-17-0, Lopinavir
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(syntactic deformable pharmaceutical foam compns.)

L2 ANSWER 26 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:521408 CAPLUS
DOCUMENT NUMBER: 137:83661
TITLE: Pharmaceutical compositions containing a non-enteric coated proton pump inhibitor and a carbonate salt and bicarbonate salt combination
INVENTOR(S): Taneja, Rajneesh; Gupta, Pramod
PATENT ASSIGNEE(S): Tap Pharmaceutical Products, Inc., USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002053097	A2	20020711	WO 2001-US48320		20011212
WO 2002053097	A3	20030130			
W: CA, JP, MX					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR					
CA 2432184	AA	20020711	CA 2001-2432184		20011212
EP 1353624	A2	20031022	EP 2001-991084		20011212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR					
JP 2004525100	T2	20040819	JP 2002-554048		20011212
PRIORITY APPLN. INFO.:			US 2000-750430	A	20001228
			WO 2001-US48320	W	20011212

AB A method for treating gastric acid disorders with a non-enteric coated proton pump inhibitor in a carrier including a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal; and a pharmaceutical composition of a non-enteric coated proton pump inhibitor in a carrier including a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal are disclosed. A preferred proton pump inhibitor is lansoprazole, a preferred bicarbonate salt is sodium bicarbonate, and a preferred carbonate salt is sodium carbonate. The composition is a fast-acting formulation which reduces the undesirable belching associated with proton pump inhibitor formulations that contain high doses of sodium bicarbonate. Granular formulations of **lansoprazole** for this example were prepared as follows. Sucrose (60 g) was dissolved in water with gentle heating to form a 60% solution Then, 46.93 g Na2CO3 and 37.17 g NaHCO3 were mixed together thoroughly. Subsequently, 35 g this mixture (carbicarb), 7.5 g lactose and 1.5 g **lansoprazole** were transferred to a mortar and mixed vigorously. The 60% sucrose solution (6 mL) was gradually added to the mortar while mixing with a pestle to form a coherent, wetted mass. This coherent mass was passed through a 10-mesh screen and the resulting granules were dried at 50° for 12 h. **Lansoprazole**, when formulated with carbicarb as granules, was **stable** in simulated gastric fluid for at least 60 min.

AB A method for treating gastric acid disorders with a non-enteric coated proton pump inhibitor in a carrier including a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal; and a pharmaceutical composition of a non-enteric coated proton pump inhibitor in a carrier including a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal are disclosed. A preferred proton pump inhibitor is **lansoprazole**, a preferred bicarbonate salt is sodium bicarbonate, and a preferred carbonate salt is sodium carbonate. The composition is a fast-acting formulation which reduces the undesirable belching associated with proton pump inhibitor formulations that contain high doses of sodium bicarbonate. Granular formulations of **lansoprazole** for this example were prepared as follows. Sucrose (60 g) was dissolved in water with gentle heating to form a 60% solution Then, 46.93 g Na2CO3 and 37.17 g NaHCO3 were mixed together thoroughly. Subsequently, 35 g this mixture (carbicarb), 7.5 g lactose and 1.5 g **lansoprazole** were transferred to a mortar and mixed vigorously. The 60% sucrose solution (6 mL) was gradually added to the mortar while mixing with a pestle to form a coherent, wetted mass. This coherent mass was passed through a 10-mesh screen and the resulting granules were dried at 50° for 12 h. **Lansoprazole**, when formulated with carbicarb as granules, was **stable** in simulated gastric fluid for at least 60 min.

IT 103577-45-3, **Lansoprazole**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals containing non-enteric coated proton pump inhibitors and carbonate salt and bicarbonate salt combination)

L2 ANSWER 27 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:314770 CAPLUS
DOCUMENT NUMBER: 136:330568
TITLE: **Stable** oral formulation containing benzimidazole derivative
INVENTOR(S): Vanderbist, Francis; Sereno, Antonio; Baudier, Philippe
PATENT ASSIGNEE(S): Galephar M/F, Belg.
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032427	A1	20020425	WO 2000-BE126	20001020
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001011213	A5	20020429	AU 2001-11213	20001020
CA 2426175	AA	20020425	CA 2001-2426175	20011018
WO 2002032425	A2	20020425	WO 2001-BE184	20011018
WO 2002032425	A3	20030116		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,				

RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002010284	A5	20020429	AU 2002-10284	20011018
EP 1326609	A2	20030716	EP 2001-978022	20011018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004043069	A1	20040304	US 2003-399482	20030418
PRIORITY APPLN. INFO.:			WO 2000-BE126 A	20001020
			WO 2001-BE184 W	20011018

AB An enteric formulation contains at least one benzimidazole derivative, said formulation comprising: a core containing at least one benzimidazole derivative and at least one lipophilic antioxidant, and an enteric envelope protecting the core at least at a pH of 3 to 5, preferably at a pH of 1 to 5. A core composition contained omeprazole, vitamin E PEG succinate, microcryst. cellulose, Crospovidone, lactose, mannitol, and Mg stearate and the coating composition contained povidone or HPMC.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Stable oral formulation containing benzimidazole derivative

ST benzimidazole oral formulation **stable**; omeprazole oral formulation **stable**

IT Granulation
(fluidized-bed; **stable** oral formulation containing benzimidazole derivative)

IT Drug delivery systems
(granules; **stable** oral formulation containing benzimidazole derivative)

IT Drug delivery systems
(oral; **stable** oral formulation containing benzimidazole derivative)

IT Antioxidants
(**stable** oral formulation containing benzimidazole derivative)

IT Disaccharides
Monosaccharides
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** oral formulation containing benzimidazole derivative)

IT Drug delivery systems
(tablets, enteric-coated; **stable** oral formulation containing benzimidazole derivative)

IT Drug delivery systems
(tablets; **stable** oral formulation containing benzimidazole derivative)

IT 12408-02-5, Hydrogen ion, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pump, inhibitors; **stable** oral formulation containing benzimidazole derivative)

IT 59-02-9, α-Tocopherol 63-42-3, Lactose 69-65-8, D-Mannitol 9002-96-4 9003-39-8, Povidone 9004-34-6, Cellulose, biological studies 9004-65-3, Hpmc 9050-31-1, HP50
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** oral formulation containing benzimidazole derivative)

IT 25212-88-8, Eudragit L30D
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**stable** oral formulation containing benzimidazole derivative)

IT 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, Lansoprazole

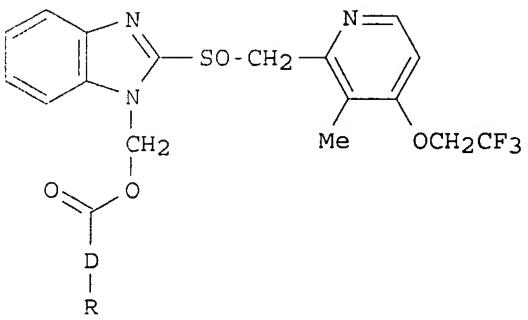
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** oral formulation containing benzimidazole derivative)

L2 ANSWER 28 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:293642 CAPLUS
DOCUMENT NUMBER: 136:325542
TITLE: Preparation of 2-[3-methyl-3-(2,2,2-trifluoroethoxy)-2-pyridylmethylsulfinyl]benzimidazole compounds as **lansoprazole** prodrugs and antiulcer agents
INVENTOR(S): Kamiyama, Keiji; Sato, Fumihiko
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030920	A1	20020418	WO 2001-JP8943	20011011
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001094228	A5	20020422	AU 2001-94228	20011011
JP 2002187890	A2	20020705	JP 2001-314204	20011011
CA 2425363	AA	20030410	CA 2001-2425363	20011011
EP 1334971	A1	20030813	EP 2001-974795	20011011
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004039027	A1	20040226	US 2003-398820	20030409

PRIORITY APPLN. INFO.: JP 2000-316864 A 20001012
WO 2001-JP8943 W 20011011

OTHER SOURCE(S): MARPAT 136:325542
GI



I

AB Compds. represented by the following general formula (I; D = O, a single bond; R = (un)substituted hydrocarbyl) or salts thereof are prepared These compds. show: (1) excellent antiulcer, gastric acid secretion inhibitory, mucosa-protecting and anti-Helicobacter pylori effects in vivo; (2) a low toxicity; (3) a high stability to acid (i.e., making it unnecessary to

process into enteric prepns., thereby saving the cost and facilitating the intake by patients with dysphagia because of the small size); (4) a higher absorption speed than enteric prepns. (i.e., achieving higher expression of the gastric acid secretion inhibitory effect); and (5) a long-lasting effect. They are highly **stable** to acid and can be converted into proton pump inhibitors (e.g. **lansoprazole**) in vivo to thereby exert an antiulcer effect. Thus, to a solution of 1.99 g [2-[3-methyl-3-(2,2,2-trifluoroethoxy)-2-pyridylmethylsulfinyl]benzimidazo l-1-yl]methanol in 25 mL THF were added 1.4 mL Et3N and 0.924 mL trimethylacetyl chloride under ice-cooling and stirred for 2.5 h under ice-cooling to give [2-[3-methyl-3-(2,2,2-trifluoroethoxy)-2-pyridylmethylsulfinyl]benzimidazol-1-yl]methyl trimethylacetate (II). The half-life of II in artificial gastric juice was 13.8 h vs. <0.03 h for **lansoprazole**. Human liver and human small intestine S9 converted II into **lansoprazole** 88.6 and 100.0%, resp.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Preparation of 2-[3-methyl-3-(2,2,2-trifluoroethoxy)-2-pyridylmethylsulfinyl]benzimidazole compounds as **lansoprazole** prodrugs and antiulcer agents

AB Compds. represented by the following general formula (I; D = O, a single bond; R = (un)substituted hydrocarbyl) or salts thereof are prepared These compds. show: (1) excellent antiulcer, gastric acid secretion inhibitory, mucosa-protecting and anti-Helicobacter pylori effects in vivo; (2) a low toxicity; (3) a high stability to acid (i.e., making it unnecessary to process into enteric prepns., thereby saving the cost and facilitating the intake by patients with dysphagia because of the small size); (4) a higher absorption speed than enteric prepns. (i.e., achieving higher expression of the gastric acid secretion inhibitory effect); and (5) a long-lasting effect. They are highly **stable** to acid and can be converted into proton pump inhibitors (e.g. **lansoprazole**) in vivo to thereby exert an antiulcer effect. Thus, to a solution of 1.99 g [2-[3-methyl-3-(2,2,2-trifluoroethoxy)-2-pyridylmethylsulfinyl]benzimidazo l-1-yl]methanol in 25 mL THF were added 1.4 mL Et3N and 0.924 mL trimethylacetyl chloride under ice-cooling and stirred for 2.5 h under ice-cooling to give [2-[3-methyl-3-(2,2,2-trifluoroethoxy)-2-pyridylmethylsulfinyl]benzimidazol-1-yl]methyl trimethylacetate (II). The half-life of II in artificial gastric juice was 13.8 h vs. <0.03 h for **lansoprazole**. Human liver and human small intestine S9 converted II into **lansoprazole** 88.6 and 100.0%, resp.

ST methyltrifluoroethoxypyridylmethylsulfinylbenzimidazole prepn
lansoprazole prodrug antiulcer; Helicobacter pylori antibacterial
lansoprazole deriv prepn; proton pump inhibitor
lansoprazole prodrug

IT Antibacterial agents
(against Helicobacter pylori; preparation of [methyl(fluoroethoxy)pyridylmet hylsulfinyl]benzimidazole compds. as **lansoprazole** prodrugs and antiulcer agents)

IT Esophagus, disease
Inflammation
(esophagitis, regurgitant; preparation of [methyl(fluoroethoxy)pyridylmethyl sulfinyl]benzimidazole compds. as **lansoprazole** prodrugs and antiulcer agents)

IT Inflammation
Stomach, disease
(gastritis; preparation of [methyl(fluoroethoxy)pyridylmethylsulfinyl]benzim idazole compds. as **lansoprazole** prodrugs and antiulcer agents)

IT Lymphoma
(mucosa-associated lymphoid tissue; preparation of [methyl(fluoroethoxy)pyridylmethylsulfinyl]benzimidazole compds. as **lansoprazole** prodrugs and antiulcer agents)

IT Dyspepsia
(non-ulcer; preparation of [methyl(fluoroethoxy)pyridylmethylsulfinyl]benzimidazole compds. as **lansoprazole** prodrugs and antiulcer agents)
IT Antacids
Antiulcer agents
Helicobacter pylori
Human
Stomach, neoplasm
(preparation of [methyl(fluoroethoxy)pyridylmethylsulfinyl]benzimidazole compds. as **lansoprazole** prodrugs and antiulcer agents)
IT Drug delivery systems
(prodrugs, for **lansoprazole**; preparation of [methyl(fluoroethoxy)pyridylmethylsulfinyl]benzimidazole compds. as **lansoprazole** prodrugs and antiulcer agents)
IT Mucous membrane
(protecting agents; preparation of [methyl(fluoroethoxy)pyridylmethylsulfinyl]benzimidazole compds. as **lansoprazole** prodrugs and antiulcer agents)
IT Gastric acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(secretion, inhibitors; preparation of [methyl(fluoroethoxy)pyridylmethylsulfinyl]benzimidazole compds. as **lansoprazole** prodrugs and antiulcer agents)
IT Digestive tract, disease
(upper gastrointestinal hemorrhage; preparation of [methyl(fluoroethoxy)pyridylmethylsulfinyl]benzimidazole compds. as **lansoprazole** prodrugs and antiulcer agents)
IT 138530-94-6P, (R)-2-[[[3-Methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-1H-benzimidazole
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of [methyl(fluoroethoxy)pyridylmethylsulfinyl]benzimidazole compds. as **lansoprazole** prodrugs and antiulcer agents)
IT 412279-40-4P, Benzoic acid [2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-1H-benzimidazol-1-yl]methyl ester 412279-41-5P, Trimethylacetic acid [2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-1H-benzimidazol-1-yl]methyl ester 412279-42-6P, Acetic acid [2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-1H-benzimidazol-1-yl]methyl ester 412279-43-7P, Phenylacetic acid [2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-1H-benzimidazol-1-yl]methyl ester 412279-44-8P 412279-45-9P, 4-Methylbenzoic acid [2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-1H-benzimidazol-1-yl]methyl ester 412279-46-0P 412279-47-1P 412279-48-2P 412279-49-3P 412279-50-6P 412279-51-7P 412279-52-8P 412279-53-9P, 4-tert-Butylbenzoic acid [2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-1H-benzimidazol-1-yl]methyl ester 412279-54-0P 412279-55-1P, Isobutyric acid [2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-1H-benzimidazol-1-yl]methyl ester 412279-56-2P, (Acetylamino)acetic acid [2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-1H-benzimidazol-1-yl]methyl ester 412279-57-3P 412279-58-4P 412279-59-5P 412279-60-8P 412279-61-9P 412279-62-0P 412279-63-1P 412279-64-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of [methyl(fluoroethoxy)pyridylmethylsulfinyl]benzimidazole compds. as **lansoprazole** prodrugs and antiulcer agents)
IT 75-36-5, Acetyl chloride 79-03-8, Propanoyl chloride 79-30-1, Isobutyryl chloride 98-88-4, Benzoyl chloride 103-80-0, Phenylacetyl chloride 108-23-6, Isopropyl chloroformate 109-61-5, Propyl

chloroformate 501-53-1, Benzyl chloroformate 541-41-3, Ethyl chloroformate 543-24-8, N-Acetylglycine 592-34-7, Butyl chloroformate 628-12-6, 2-Methoxyethyl chloroformate 874-60-2, 4-Methylbenzoyl chloride 1710-98-1, 4-tert-Butylbenzoyl chloride 3282-30-2, Trimethylacetyl chloride 103577-40-8, 2-[[[3-Methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]thio]-1H-benzimidazole 103577-45-3, 2-[[[3-Methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-1H-benzimidazole
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of [methyl(fluoroethoxy)pyridylmethylsulfinyl]benzimidazole compds. as **lansoprazole** prodrugs and antiulcer agents)

IT 412279-65-3P, [2-[[[3-Methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-1H-benzimidazol-1-yl]methanol 412279-66-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of [methyl(fluoroethoxy)pyridylmethylsulfinyl]benzimidazole compds. as **lansoprazole** prodrugs and antiulcer agents)

IT 103577-45-3DP, **Lansoprazole**, derivs.
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prodrugs for; preparation of [methyl(fluoroethoxy)pyridylmethylsulfinyl]benzimidazole compds. as **lansoprazole** prodrugs and antiulcer agents)

IT 9000-83-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proton-translocating, inhibitors; preparation of [methyl(fluoroethoxy)pyridylmethylsulfinyl]benzimidazole compds. as **lansoprazole** prodrugs and antiulcer agents)

L2 ANSWER 29 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:256025 CAPLUS
DOCUMENT NUMBER: 136:284447
TITLE: Proton pump inhibitor formulation
INVENTOR(S): Cullen, Dan; Pelloni, Christopher L.
PATENT ASSIGNEE(S): Geneva Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002026210	A2	20020404	WO 2001-US42298		20010925
WO 2002026210	A3	20021219			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2001096908	A5	20020408	AU 2001-96908		20010925
US 2002064555	A1	20020530	US 2001-962785		20010925
US 2003211147	A1	20031113	US 2003-458776		20030609
PRIORITY APPLN. INFO.:			US 2000-236993P	P	20000929
			US 2001-962785	A1	20010925
			WO 2001-US42298	W	20010925

OTHER SOURCE(S): MARPAT 136:284447

AB Pharmaceutical capsule dosage forms of benzimidazole proton pump inhibitors are prepared by enclosing one or several enteric coated compressed cores in a capsule shell. The inventive formulations are **stable** and have higher bioavailability of the active ingredient relative to pellet and granule containing formulations. A core composition contained omeprazole 10.00, anhydrous lactose 36.95, microcryst. cellulose 9.0, Na lauryl sulfate 1.2, and croscarmellose sodium 2.25 mg, and the enteric coating contained Eudragit L30D55 4.104 and PEG 0.213 mg.

AB Pharmaceutical capsule dosage forms of benzimidazole proton pump inhibitors are prepared by enclosing one or several enteric coated compressed cores in a capsule shell. The inventive formulations are **stable** and have higher bioavailability of the active ingredient relative to pellet and granule containing formulations. A core composition contained omeprazole 10.00, anhydrous lactose 36.95, microcryst. cellulose 9.0, Na lauryl sulfate 1.2, and croscarmellose sodium 2.25 mg, and the enteric coating contained Eudragit L30D55 4.104 and PEG 0.213 mg.

IT 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 104340-86-5, Leminoprazole 117976-89-3, Rabeprazole 117976-90-6, Pariprazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(proton pump inhibitor formulation)

L2 ANSWER 30 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:185616 CAPLUS
DOCUMENT NUMBER: 136:252482
TITLE: Preparation of aqueous clear solution dosage forms with bile acids
INVENTOR(S): Yoo, Seo Hong
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 35 pp., Cont.-in-part of U. S. 6,251,428.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002031558	A1	20020314	US 2001-778154		20010205
US 6251428	B1	20010626	US 1999-357549		19990720
US 2003186933	A1	20031002	US 2002-309603		20021204
PRIORITY APPLN. INFO.:			US 1998-94069P	P	19980724
			US 1999-357549	A2	19990720
			US 2000-180268P	P	20000204
			US 2001-778154	A3	20010205

AB Compns. for pharmaceutical and other uses comprise clear aqueous solns. of bile acids which do not form any detectable ppts. over selected ranges of pH values of the aqueous solution The compns. comprise (i) water, (ii) a bile acid component in the form of a bile acid, bile acid salt, or a bile acid conjugated with an amine by an amide linkage; and (iii) either or both an aqueous soluble starch conversion product and an aqueous soluble non-starch polysaccharide. The composition remains in solution without forming a precipitate over a range of pH values and, according to one embodiment, remains in solution for all pH values obtainable in an aqueous system. The composition may further contain a pharmaceutical compound, such as insulin, heparin, bismuth compds., amantadine and rimantadine. For example, solution dosage forms that did not show any precipitation at any pH were prepared containing ursodeoxycholic acid (UDCA) 22

Ibuprofen 15826-37-6, Cromolyn sodium 18559-94-9, Albuterol 19237-84-4, Prazosin hydrochloride 19794-93-5, Trazodone 21829-25-4, Nifedipine 22204-53-1, Naproxen 22254-24-6, Ipratropium bromide 22494-42-4, Diflunisal 22916-47-8, Miconazole 23031-32-5, Terbutaline sulfate 23593-75-1, Clotrimazole 24169-02-6, Econazole nitrate 25717-80-0, Molsidomine 26787-78-0, Amoxicillin 28300-74-5, Antimony potassium tartrate 29094-61-9, Glipizide 30392-40-6, Bitolterol 30516-87-1, Zidovudine 31586-77-3, Bismuth sodium tartrate 32222-06-3, Calcitriol 34031-32-8, Auranofin 35711-34-3, Tolmetin sodium 36322-90-4, Piroxicam 36703-88-5, Isoprinosine 36791-04-5, Ribavirin 38260-01-4, Trientine hydrochloride 38304-91-5, Minoxidil 38677-81-5, Pirbuterol 39809-25-1, Penciclovir 42399-41-7, Diltiazem 50370-12-2, Cefadroxil 51110-01-1, Somatostatin 51333-22-3, Budesonide 51481-61-9, Cimetidine 53678-77-6, Muramyl dipeptide 53994-73-3, Cefaclor 54182-58-0, Sucralfate 56180-94-0, Acarbose 59122-46-2, Misoprostol 59277-89-3, Acyclovir 61318-91-0, Sulconazole nitrate 63074-08-8, Terazosin hydrochloride 63585-09-1, Foscarnet sodium 63675-72-9, Nisoldipine 64211-46-7, Oxiconazole nitrate 64706-54-3, Bepridil 65277-42-1, Ketoconazole 66357-35-5, Ranitidine 66357-59-3, Ranitidine hydrochloride 69655-05-6, Didanosine 73590-58-6, Omeprazole 75330-75-5, Lovastatin 75695-93-1, Isradipine 76824-35-6, Famotidine 76963-41-2, Nizatidine 77883-43-3, Doxazosin mesylate 78628-80-5, Terbinafine hydrochloride 79902-63-9, Simvastatin 80474-14-2, Fluticasone propionate 81103-11-9, Clarithromycin 81131-70-6, Pravastatin sodium 83150-76-9, Octreotide 83881-52-1, Cetirizine dihydrochloride 83905-01-5, Azithromycin 84625-61-6, Itraconazole 86386-73-4, Fluconazole 89365-50-4, Salmeterol 91980-85-7 93957-55-2, Fluvastatin sodium 95233-18-4, Atovaquone 103577-45-3, Lansoprazole 104227-87-4, Famciclovir 107753-78-6, Zafirlukast 107910-75-8, Ganciclovir sodium 111406-87-2, Zileuton 113852-37-2, Cidofovir 124832-27-5, Valacyclovir hydrochloride 129618-40-2, Nevirapine 133107-64-9, Insulin lispro 134523-03-8, Atorvastatin-calcium 134678-17-4, Lamivudine 135062-02-1, Repaglinide 139755-83-2, Sildenafil 143201-11-0, Cerivastatin sodium 147221-93-0, Delavirdine mesylate 149845-06-7, Saquinavir mesylate 151767-02-1, Montelukast sodium 155213-67-5, Ritonavir 157810-81-6, Indinavir sulfate 159989-65-8, Nelfinavir mesylate 171599-83-0, Sildenafil citrate 403804-21-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **stable** aqueous solns. containing bile acids for therapy)

IT 50-21-5, Lactic acid, reactions 56-87-1, L-Lysine, reactions 60-00-4, Edetic acid, reactions 62-49-7, Choline 70-26-8, L-Ornithine 74-79-3, L-Arginine, reactions 77-92-9, Citric acid, reactions 87-69-4, Tartaric acid, reactions 102-71-6, Triethanolamine, reactions 110-85-0, Piperazine, reactions 110-85-0D, Piperazine, N-alkyl derivs. 110-89-4, Piperidine, reactions 110-89-4D, Piperidine, N-alkyl derivs. 110-91-8, Morpholine, reactions 110-91-8D, Morpholine, N-alkyl derivs. 111-40-0, Diethylene triamine 112-57-2, Tetraethylene pentamine 123-75-1, Pyrrolidine, reactions 488-43-7, D-Glucamine 6915-15-7, Malic acid 7664-41-7, Ammonia, reactions 14002-32-5, Trimethanolamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **stable** aqueous solns. containing bile acids for therapy)

IT 50-99-7, D-Glucose, biological studies 9004-53-9, Dextrin 9004-54-0, Dextran, biological studies 9005-25-8, Starch, biological studies 9050-36-6, Maltodextrin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **stable** aqueous solns. containing bile acids for therapy)

L2 ANSWER 31 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:717301 CAPLUS
DOCUMENT NUMBER: 135:278020

10/773,535

TITLE: Storage-**stable** benzimidazole tablets and their manufacture
INVENTOR(S): Moroshima, Kenji; Kimura, Susumu; Shimogaki, Norio; Narasaki, Ryuichi; Funabashi, Hiroshi; Fujioka, Masaru; Ando, Hidenobu; Aoki, Shigeru; Iwamoto, Kiyoshi
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001270827	A2	20011002	JP 2000-81276	20000323

PRIORITY APPLN. INFO.: JP 2000-81276 20000323
OTHER SOURCE(S): MARPAT 135:278020
AB The tablets contain benzimidazoles Het1SOCH2Het2 [Het1 = (un)substituted benzimidazol-2-yl; Het2 = (un)substituted 2-pyridyl] or their physiol. acceptable salts, crospovidone (I), and lubricants except Mg stearate. Tablets containing rabeprazole Na 20.0, mannitol 83.8, I 40.0, NaOH 1.0, hydroxypropyl cellulose 3.0, and Na stearyl fumarate 2.2 mg showed disintegration time 6.5-7.4 and 6.2-7.4 before and after 2-day storage at 60°, resp.
TI Storage-**stable** benzimidazole tablets and their manufacture
IT Antiulcer agents
Lubricants
(storage-**stable** benzimidazole tablets containing crospovidone and lubricants)
IT Drug delivery systems
(tablets, enteric-coated; storage-**stable** benzimidazole tablets containing crospovidone and lubricants)
IT Drug delivery systems
(tablets; storage-**stable** benzimidazole tablets containing crospovidone and lubricants)
IT 57-11-4, Stearic acid, biological studies 1310-73-2, Sodium hydroxide, biological studies 1592-23-0, Calcium stearate 4070-80-8, Sodium stearyl fumarate 9003-39-8D, crosslinked 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 117976-89-3, Rabeprazole 117976-90-6, Rabeprazole sodium
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(storage-**stable** benzimidazole tablets containing crospovidone and lubricants)

L2 ANSWER 32 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:635890 CAPLUS
DOCUMENT NUMBER: 135:185502
TITLE: Orally administrable acid-**stable** antiulcer benzimidazole polymeric derivatives
INVENTOR(S): Mali, Subhash; Gupte, Rajan; Deshpande, Jayant; Ranbhan, Kamlesh
PATENT ASSIGNEE(S): Kopran Research Laboratories Limited, India
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062248	A1	20010830	WO 2000-IN16	20000224
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2400953	AA	20010830	CA 2000-2400953	20000224
EP 1257269	A1	20021120	EP 2000-939036	20000224
EP 1257269	B1	20041103		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003523386	T2	20030805	JP 2001-561314	20000224
BR 2000017140	A	20040525	BR 2000-17140	20000224
AT 281164	E	20041115	AT 2000-939036	20000224
US 2002038032	A1	20020328	US 2001-964442	20010928
US 2003023091	A9	20030130		
US 6617338	B2	20030909		
ZA 2002006649	A	20030820	ZA 2002-6649	20020820
PRIORITY APPLN. INFO.:			WO 2000-IN16 W	20000224

OTHER SOURCE(S): MARPAT 135:185502

AB Orally administrable acid **stable** anti-ulcer benzimidazole derivs. which are polymer based, are prepared The process of preparation comprises condensing a benzimidazole with a biocompatible partially orally biodegradable synthetic crosslinked polymer in aqueous medium at 5-80° and pH 4-11 under an inert atmospheric The percent weight of benzimidazole with respect to the polymeric conjugate is 1-50. The reaction mixture is cooled and the product is isolated and dried at 25-45°. There is also provided a formulation of the polymeric benzimidazoles in combination with excipients. Thus, a copolymer from acrylamide and glycidyl methacrylate was allowed to react with omeprazole to give a polymer-substituted drug. Tablet contained the above polymer-substituted omeprazole 100.0, lactose 70.0, Mg stearate 1.5, Me cellulose 0.6, and crospovidone 5.5 g, and water qs.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Orally administrable acid-**stable** antiulcer benzimidazole polymeric derivatives

AB Orally administrable acid **stable** anti-ulcer benzimidazole derivs. which are polymer based, are prepared The process of preparation comprises condensing a benzimidazole with a biocompatible partially orally biodegradable synthetic crosslinked polymer in aqueous medium at 5-80° and pH 4-11 under an inert atmospheric The percent weight of benzimidazole with respect to the polymeric conjugate is 1-50. The reaction mixture is cooled and the product is isolated and dried at 25-45°. There is also provided a formulation of the polymeric benzimidazoles in combination with excipients. Thus, a copolymer from acrylamide and glycidyl methacrylate was allowed to react with omeprazole to give a polymer-substituted drug. Tablet contained the above polymer-substituted omeprazole 100.0, lactose 70.0, Mg stearate 1.5, Me cellulose 0.6, and crospovidone 5.5 g, and water qs.

IT Drug delivery systems
(capsules; orally administrable acid-**stable** antiulcer benzimidazole polymeric derivs.)

IT Antiulcer agents

(orally administrable acid-**stable** antiulcer benzimidazole polymeric derivs.)
IT Drug delivery systems
(suspensions; orally administrable acid-**stable** antiulcer benzimidazole polymeric derivs.)
IT Drug delivery systems
(tablets; orally administrable acid-**stable** antiulcer benzimidazole polymeric derivs.)
IT 51-17-2DP, benzimidazole, derivs. 31743-77-8DP, Ethylene glycol dimethacrylate-glycidyl methacrylate copolymer, reaction products with imidazoles 55031-95-3DP, Acrylamide-glycidyl methacrylate copolymer, reaction products with imidazoles 73590-58-6DP, Omeprazole, reaction products with polymers 85075-35-0DP, Acrylonitrile-ethylene glycol dimethacrylate-glycidyl acrylate copolymer, reaction products with imidazoles 102625-70-7DP, Pantoprazole, reaction products with polymers 103577-45-3DP, **Lansoprazole**, reaction products with polymers
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(orally administrable acid-**stable** antiulcer benzimidazole polymeric derivs.)

L2 ANSWER 33 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:450876 CAPLUS
DOCUMENT NUMBER: 135:51076
TITLE: New **stable** multi-unitary pharmaceutical preparations containing substituted benzimidazoles
INVENTOR(S): Goncalves Mendes, Carla Patricia; Caeiro Ramalho De Oliveira, Maria Julia
PATENT ASSIGNEE(S): Laboratorio Medinfar-Produtos Farmaceuticos, S.A., Port.
SOURCE: Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1108425	A1	20010620	EP 1999-670010	19991216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6379705	B1	20020430	US 2000-580551	20000530

PRIORITY APPLN. INFO.: EP 1999-670010 A 19991216
AB The present invention relates to new oral multi-unitary pharmaceutical prepns. containing substituted benzimidazoles as inhibitors of H+,K+-ATPase (i.e., omeprazole, **lansoprazole**, pantoprazole, leminoprazole and pariprazole) or their pharmaceutically acceptable salts. Such pharmaceutical prepns. are **stable** pellet prepns. containing substituted benzimidazole(s) or their salts and they comprise a quantity of active ingredient of 1-50 mg, an inert core of spherical symmetry with a diameter of 600-1000 μm, constituted by inert excipients, coated with an active layer containing at least one substituted benzimidazole in the micronized form and various pharmaceutically acceptable inert excipients, mixed in suitable proportions in order to allow the disaggregation of the formulations and dissoln. of the active ingredient(s) in an appropriate manner, coated in turn with an insulating layer of a polymer soluble in water, free from alkaline and/or alkaline-earthy metallic salts, of a min. thickness of 15 μm, this layer being coated lastly with a gastro-resistant or enteric layer of a min. thickness of 30 μm. This invention also refers to the process for the preparation of said pharmaceutical

prepns.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI New stable multi-unitary pharmaceutical preparations containing substituted benzimidazoles
AB The present invention relates to new oral multi-unitary pharmaceutical prepns. containing substituted benzimidazoles as inhibitors of H+,K+-ATPase (i.e., omeprazole, **lansoprazole**, pantoprazole, leminoprazole and pariprazole) or their pharmaceutically acceptable salts. Such pharmaceutical prepns. are **stable** pellet prepns. containing substituted benzimidazole(s) or their salts and they comprise a quantity of active ingredient of 1-50 mg, an inert core of spherical symmetry with a diameter of 600-1000 μm, constituted by inert excipients, coated with an active layer containing at least one substituted benzimidazole in the micronized form and various pharmaceutically acceptable inert excipients, mixed in suitable proportions in order to allow the disaggregation of the formulations and dissoln. of the active ingredient(s) in an appropriate manner, coated in turn with an insulating layer of a polymer soluble in water, free from alkaline and/or alkaline-earthy metallic salts, of a min. thickness of 15 μm, this layer being coated lastly with a gastro-resistant or enteric layer of a min. thickness of 30 μm. This invention also refers to the process for the preparation of said pharmaceutical prepns.
IT 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 104340-86-5, Leminoprazole 117976-89-3, Pariprazole
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of multi-unitary enteric-coated pellet prepns. containing substituted benzimidazoles)

L2 ANSWER 34 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:116909 CAPLUS
DOCUMENT NUMBER: 134:125786
TITLE: Comparison of 24-hour intragastric pH using four liquid formulations of **lansoprazole** and omeprazole. [Erratum to document cited in CA132:44775]
AUTHOR(S): Sharma, Virender K.
CORPORATE SOURCE: Division of Gastroenterology, University of Arkansas for Medical Sciences, Little Rock, AR, 72205-7199, USA
SOURCE: American Journal of Health-System Pharmacy (2000), 57(7), 699
CODEN: AHSPEK; ISSN: 1079-2082
PUBLISHER: American Society of Health-System Pharmacists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB On page S21, in the first full paragraph, the third sentence should read as follows: "Quercia and colleagues17 found that simplified omeprazole suspension 2 mg/mL was **stable** for up to 14 days at room temperature and for 30 days when refrigerated or frozen.".
TI Comparison of 24-hour intragastric pH using four liquid formulations of lansoprazole and omeprazole. [Erratum to document cited in CA132:44775]
AB On page S21, in the first full paragraph, the third sentence should read as follows: "Quercia and colleagues17 found that simplified omeprazole suspension 2 mg/mL was **stable** for up to 14 days at room temperature and for 30 days when refrigerated or frozen.".
ST erratum **lansoprazole** omeprazole intragastric pH; **lansoprazole** omeprazole intragastric pH erratum
IT Antacids
pH

(comparison of 24-h intragastric pH using four liquid formulations of **lansoprazole** and omeprazole (Erratum))

IT Gastric acid
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(comparison of 24-h intragastric pH using four liquid formulations of **lansoprazole** and omeprazole (Erratum))

IT 73590-58-6, Omeprazole 103577-45-3, **Lansoprazole**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of 24-h intragastric pH using four liquid formulations of **lansoprazole** and omeprazole (Erratum))

IT 9000-83-3, ATPase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hydrogen ion-translocating, inhibitors; comparison of 24-h intragastric pH using four liquid formulations of **lansoprazole** and omeprazole (Erratum))

L2 ANSWER 35 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:911051 CAPLUS
DOCUMENT NUMBER: 134:61541
TITLE: **Stable** benzimidazole formulation
INVENTOR(S): Lahav, Raffael; Azoulay, Valerie
PATENT ASSIGNEE(S): Dexcel Ltd., Israel
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078284	A1	20001228	WO 2000-IL364	20000621
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2377605	AA	20001228	CA 2000-2377605	20000621
EP 1187599	A1	20020320	EP 2000-939023	20000621
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: IL 1999-130602 A 19990622
WO 2000-IL364 W 20000621

AB A stable composition with a benzimidazole derivative, such as omeprazole, which does not contain a separating layer between the active compound and an enteric coating layer is described. Instead, the enteric coating layer is applied as a solution with a pH value of at least 6.5, and more preferably in a range of from about 7 to about 10, directly to the benzimidazole derivative substrate. This solution, with the optional addition of a plasticizer, can be directly coated onto the substrate without any necessity for an intermediate layer. Furthermore, in this pH range, the enteric coating is optionally applicable in an aqueous solution, thereby obviating the need for organic solvents for dissolving the enteric coating material. The resultant formulation maintains the stability of the benzimidazole derivative during

storage and at the same time protects the product during passage through the acidic environment of the stomach. The problem of interaction between the enteric coat and the alkaline core is thus completely eliminated as the enteric coat at this stage is no longer acidic. Thus, an active tablet core contained omeprazole 20, lactose 192.5, MgCO3 10, sodium starch glycolate 10, Povidone 10, and sodium stearyl fumarate 7.5 mg. The enteric coating layer comprised HPMCAS 16.1, tri-Et citrate 4.5, sodium lauryl sulfate 0.5, talc 8.04, and NaOH 0.86 mg.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI **Stable** benzimidazole formulation

AB A **stable** composition with a benzimidazole derivative, such as omeprazole, which does not contain a separating layer between the active compound and an enteric coating layer is described. Instead, the enteric coating layer is applied as a solution with a pH value of at least 6.5, and more preferably in a range of from about 7 to about 10, directly to the benzimidazole derivative substrate. This solution, with the optional addition of a plasticizer, can be directly coated onto the substrate without any necessity for an intermediate layer. Furthermore, in this pH range, the enteric coating is optionally applicable in an aqueous solution, thereby obviating the need for organic solvents for dissolving the enteric coating material. The resultant formulation maintains the stability of the benzimidazole derivative during storage and at the same time protects the product during passage through the acidic environment of the stomach. The problem of interaction between the enteric coat and the alkaline core is thus completely eliminated as the enteric coat at this stage is no longer acidic. Thus, an active tablet core contained omeprazole 20, lactose 192.5, MgCO3 10, sodium starch glycolate 10, Povidone 10, and sodium stearyl fumarate 7.5 mg. The enteric coating layer comprised HPMCAS 16.1, tri-Et citrate 4.5, sodium lauryl sulfate 0.5, talc 8.04, and NaOH 0.86 mg.

IT Drug delivery systems
(beads; **stable** benzimidazole formulation)

IT Drug delivery systems
(enteric-coated; **stable** benzimidazole formulation)

IT Drug delivery systems
(pellets, enteric-coated; **stable** benzimidazole formulation)

IT Drug delivery systems
(pellets; **stable** benzimidazole formulation)

IT Compression
Dissolution rate
Drug bioavailability
Plasticizers
Spheronization
(**stable** benzimidazole formulation)

IT Drug delivery systems
(tablets, enteric-coated; **stable** benzimidazole formulation)

IT Drug delivery systems
(tablets; **stable** benzimidazole formulation)

IT 73590-58-6, Omeprazole
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**stable** benzimidazole formulation)

IT 51-17-2D, Benzimidazole, derivs. 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 104340-86-5, Leminoprazole 117976-89-3, Rabeprazole
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** benzimidazole formulation)

IT 68-04-2, Trisodium citrate 77-92-9D, Citric acid, esters 77-93-0, Triethyl citrate 88-99-3D, Phthalic acid, esters 1310-58-3, Potassium

hydroxide (K(OH)), biological studies 1310-73-2, Sodium hydroxide (Na(OH)), biological studies 1336-21-6, Ammonium hydroxide ((NH4)(OH)) 9004-38-0, Cellulose acetate phthalate 9050-31-1, Hydroxypropyl methyl cellulose phthalate 25086-15-1, Methacrylic acid-Methyl methacrylate copolymer 28572-98-7, Methacrylic acid-ethyl methacrylate copolymer 52907-01-4, Cellulose acetate trimellitate 53237-50-6 71138-97-1, Hydroxypropyl methyl cellulose acetate succinate 106392-12-5, Poloxamer
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** benzimidazole formulation)

L2 ANSWER 36 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:840390 CAPLUS
DOCUMENT NUMBER: 135:40734
TITLE: Safety review in 10,008 users of **lansoprazole** in daily practice
AUTHOR(S): Claessens, Angela A. M. C.; Heerdink, Eibert R.; Van Eijk, Jacques Th. M.; Lamers, Cornelis B. H. W.; Leufkens, Hubert G. M.
CORPORATE SOURCE: Department of Pharmacoepidemiology and Pharmacotherapy, Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht, 3508 TB, Neth.
SOURCE: Pharmacoepidemiology and Drug Safety (2000), 9(5), 383-391
CODEN: PDSAEA; ISSN: 1053-8569
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Soon after the introduction of the proton pump inhibitor, **lansoprazole**, a 4-yr observational follow-up study was started to evaluate the safety of this drug in naturally-occurring groups of patients in The Netherlands. Results of this study were compared with clin. trial data and the limited published data from observational studies. A prospective, observational study in which patients with a new episode of lansoprazole use were followed during the medication period for a maximum of 2 yr. All (adverse) events during use were documented by the prescriber, irresp. of possible association with **lansoprazole** therapy. A total of 805 general practitioners (GPs) and 266 specialists provided a total of 10,008 **lansoprazole** users with a broad range of diagnoses. Of all patients, 17.4% reported one or more adverse events. The profile and frequency of reported adverse events was consistent with results from clin. trials and other observational studies. The most frequently reported adverse events were diarrhoea, headache, nausea, skin disorders, dizziness and generalized abdominal pain/cramps. There was no new evidence of rare adverse events. Furthermore, no **lansoprazole** -related unlabeled adverse events of clin. significance were recorded. Although the patterns of use of **lansoprazole** in daily practice deviated to some extent from the diagnoses in the information leaflet, **lansoprazole** was found to have a highly acceptable safety profile in this large naturally-occurring group of users. Reporting rates were higher soon after introduction of **lansoprazole** before falling to a lower **stable** level.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Safety review in 10,008 users of **lansoprazole** in daily practice
AB Soon after the introduction of the proton pump inhibitor, **lansoprazole**, a 4-yr observational follow-up study was started to evaluate the safety of this drug in naturally-occurring groups of patients in The Netherlands. Results of this study were compared with clin. trial data and the limited published data from observational studies. A prospective, observational study in which patients with a new episode of **lansoprazole** use were followed during the medication period for a maximum of 2 yr. All (adverse) events during use were documented by the

prescriber, irresp. of possible association with **lansoprazole** therapy. A total of 805 general practitioners (GPs) and 266 specialists provided a total of 10,008 **lansoprazole** users with a broad range of diagnoses. Of all patients, 17.4% reported one or more adverse events. The profile and frequency of reported adverse events was consistent with results from clin. trials and other observational studies. The most frequently reported adverse events were diarrhoea, headache, nausea, skin disorders, dizziness and generalized abdominal pain/cramps. There was no new evidence of rare adverse events. Furthermore, no **lansoprazole** -related unlabeled adverse events of clin. significance were recorded. Although the patterns of use of **lansoprazole** in daily practice deviated to some extent from the diagnoses in the information leaflet, **lansoprazole** was found to have a highly acceptable safety profile in this large naturally-occurring group of users. Reporting rates were higher soon after introduction of **lansoprazole** before falling to a lower **stable** level.

ST **lansoprazole** safety adverse event

IT 9000-83-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(proton-translocating, inhibitor; safety review in 10,008 users of **lansoprazole** in daily practice)

IT 103577-45-3, **Lansoprazole**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(safety review in 10,008 users of **lansoprazole** in daily practice)

L2 ANSWER 37 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:579978 CAPLUS
DOCUMENT NUMBER: 133:256898
TITLE: Spectrophotometric assay of **lansoprazole** in pharmaceutical dosage formulations
AUTHOR(S): Rajput, Sadhana J.; Patel, Kalpana G.
CORPORATE SOURCE: Pharmacy Department, Faculty of Techno. & Eng., M.S. University of Baroda, Vadodara, 390 001, India
SOURCE: Eastern Pharmacist (2000), 43(506), 101-102
CODEN: EAPHA6; ISSN: 0012-8872
PUBLISHER: Eastern Pharmacist
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two spectrophotometric methods (I and II) for the determination of **lansoprazole** were developed. Method I is based on ion-pair extraction spectrophotometry as **lansoprazole** can form an extractable ion-pair complex with bromocresol green (BCG). The chromogen shows maximum absorbance at 420 nm and **stable** for 2 h. The Beer's law was obeyed in the concentration range 1 to 20 mcg/mL and reproducibility of the method in method II, the chromogen, obtained after dissolving **lansoprazole** in an acidic solvent, shows the absorption maximum at 410 nm. Beer's law range was obtained in the concentration range 5 to 70 mcg/mL.
Both the methods were used to analyze the **lansoprazole** in its capsule formulations and the results obtained are in good agreement with the labeled amts.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Spectrophotometric assay of **lansoprazole** in pharmaceutical dosage formulations

AB Two spectrophotometric methods (I and II) for the determination of **lansoprazole** were developed. Method I is based on ion-pair extraction

spectrophotometry as **lansoprazole** can form an extractable ion-pair complex with bromocresol green (BCG). The chromogen shows maximum absorbance at 420 nm and **stable** for 2 h. The Beer's law was obeyed in the concentration range 1 to 20 mcg/mL and reproducibility of the method in method II, the chromogen, obtained after dissolving **lansoprazole** in an acidic solvent, shows the absorption maximum at 410 nm. Beer's law range was obtained in the concentration range 5 to 70 mcg/mL.

Both the methods were used to analyze the **lansoprazole** in its capsule formulations and the results obtained are in good agreement with the labeled amts.

ST **lansoprazole** detn spectroscopy bromocresol green

IT Spectrophotometry
(spectrophotometric assay of **lansoprazole** in pharmaceutical dosage formulations)

IT 103577-45-3, **Lansoprazole**
RL: ANT (Analyte); ANST (Analytical study)
(spectrophotometric assay of **lansoprazole** in pharmaceutical dosage formulations)

IT 76-60-8, Bromocresol green
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(spectrophotometric assay of **lansoprazole** in pharmaceutical dosage formulations)

L2 ANSWER 38 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:475425 CAPLUS
DOCUMENT NUMBER: 133:94537
TITLE: Pharmaceutical formulations containing inclusion amino acid salts compounds of benzimidazole derivatives with cyclodextrins
INVENTOR(S): Mendes Cerdeira, Ana Maria; De Sousa Goucha, Jorge Pedro Manuel
PATENT ASSIGNEE(S): Tecnimede-Sociedade Tecnico-Medicinal, S.A., Port.
SOURCE: Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1018340	A1	20000712	EP 1999-670003	19990106
EP 1018340	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 249218	E	20030915	AT 1999-670003	19990106
PT 1018340	T	20031231	PT 1999-670003	19990106
ES 2149750	T3	20040601	ES 1999-670003	19990106

PRIORITY APPLN. INFO.: EP 1999-670003 A 19990106

AB The present invention concerns new very **stable** inclusion compds. from a hydrosol. basic amino acid salt of a benzimidazole derivative, namely omeprazole, **lansoprazole** and pantoprazole, and one or more cyclodextrins, preferably β-cyclodextrin; the process of their preparation, and their use in the manufacture of a medicine for the prophylactic and therapeutic treatment of duodenal gastric ulcer, gastro esophageal reflow disease and Zollinger-Ellison-syndrome are also disclosed. To a solution of 7.4 g L-arginine in 200 mL of water was added 3.0 g omeprazole followed by addition of 2.68 g of β-cyclodextrin and stirred for 2 h. After the lyophilization, the resulting inclusion compound (1:5:2) was kept at 40° and 75% RH for 6 mo to show degradation products of 0.8%. A tablet

contained the above inclusion compound 86.8, microcryst. cellulose 213.0, colloidal silica 3.0, and magnesium stearate 3.0 g.

AB The present invention concerns new very **stable** inclusion compds. from a hydrosol. basic amino acid salt of a benzimidazole derivative, namely omeprazole, **lansoprazole** and pantoprazole, and one or more cyclodextrins, preferably β-cyclodextrin; the process of their preparation, and their use in the manufacture of a medicine for the prophylactic and therapeutic treatment of duodenal gastric ulcer, gastro esophageal reflow disease and Zollinger-Ellison-syndrome are also disclosed. To a solution of 7.4 g L-arginine in 200 mL of water was added 3.0 g omeprazole followed by addition of 2.68 g of β-cyclodextrin and stirred for 2 h. After the lyophilization, the resulting inclusion compound (1:5:2) was kept at 40° and 75% RH for 6 mo to show degradation products of 0.8%. A tablet contained the above inclusion compound 86.8, microcryst. cellulose 213.0, colloidal silica 3.0, and magnesium stearate 3.0 g.

L2 ANSWER 39 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:407807 CAPLUS

DOCUMENT NUMBER: 133:12609

TITLE: Superiority of **lansoprazole** vs. ranitidine in healing nonsteroidal anti-inflammatory drug-associated gastric ulcers; results of a double-blind, randomized, multicenter study

AUTHOR(S): Agrawal, Naurang M.; Campbell, Donald R.; Safdi, Michael A.; Lukasik, Nancy L.; Huang, Bidan; Haber, Marian M.; Bailey, Robert J.; Barish, Charles F.; Bianci, Thomas; Birbara, Charles Allen; Bird, Phillip C.; Breiter, Jeffrey R.; Cheng, Edward; Collip, Charles; Davis, Carleton; DeMicco, Michael; Doyle, James; Fleischmann, Roy; Gaddam, Syam P.; Harford, William; Ho, Samuel; Hussey, Keith P.; Jones, James V.; Khandelwal, Mukul; Kogut, David G.; Krause, Richard; Krumholz, Steven; Maton, Paul N.; McElroy, Aubrey; Moskovitz, Morry; Ondrejicka, John, Jr.; Pambianco, Daniel; Ponich, Terry; Pruitt, Ronald E.; Robinson, Malcom; Sabesin, Seymour; Sahba, Bruce; Schwartz, Howard I.; Schwartz, Jerrold; Shah, Nayan R.; Silvers, David; Sontag, Stephen; Strong, Lewis; Winkle, Peter; Winston, Barry; Wolosin, James

CORPORATE SOURCE: NSAID-Associated Gastric Ulcer Study Group, Department of Medicine, University of Connecticut Health Center, Farmington, CT, USA

SOURCE: Archives of Internal Medicine (2000), 160(10), 1455-1461
CODEN: AIMDAP; ISSN: 0003-9926

PUBLISHER: American Medical Association

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: The usefulness of nonsteroidal anti-inflammatory drugs (NSAIDs) is limited by adverse gastrointestinal tract events. Objective: To identify the optimal antisecretory therapy for healing of gastric ulcer in patients using NSAIDs and the impact of concurrent Helicobacter pylori infection on ulcer healing. Design: Prospective, double-blind, multicenter, parallel-group study. Setting: Gastroenterol. practices in ambulatory and referral center settings. Patients: Three hundred fifty-three patients with an active, nonmalignant gastric ulcer at least 5 mm in diameter confirmed by endoscopy and biopsy and who continued to receive **stable** doses of NSAIDs. Intervention: Patients were randomized to receive ranitidine hydrochloride, 150 mg twice daily, or lansoprazole, 15 mg or 30 mg once daily, for 8 wk. Measurements: Healing was assessed by endoscopy at 4 and 8 wk in an intent-to-treat

population. Helicobacter pylori status was assessed by histol. examination Results: After 8 wk of treatment, healing was observed in 61 (53%) of 115, 81 (69%) of 118, and 85 (73%) of 117 patients receiving ranitidine **lansoprazole**, 15 mg, and **lansoprazole**, 30 mg, resp. (P<.05 for ranitidine vs. both **lansoprazole** doses; 95% confidence interval, 3.2-28.0 for ranitidine vs. **lansoprazole**, 15 mg, and 7.4-31.8 for ranitidine vs. **lansoprazole**, 30 mg). The gastric ulcer healing rates were similar between H pylori-infected and -noninfected patients, with a statistically significant increase with the use of **lansoprazole** vs. ranitidine. Conclusions: In patients who require continuous treatment with NSAIDs, **lansoprazole** is superior to ranitidine for healing of NSAID-associated gastric ulcers. Healing is not delayed by the presence of H pylori infection.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Superiority of **lansoprazole** vs. ranitidine in healing nonsteroidal anti-inflammatory drug-associated gastric ulcers; results of a double-blind, randomized, multicenter study

AB Background: The usefulness of nonsteroidal anti-inflammatory drugs (NSAIDs) is limited by adverse gastrointestinal tract events. Objective: To identify the optimal antisecretory therapy for healing of gastric ulcer in patients using NSAIDs and the impact of concurrent Helicobacter pylori infection on ulcer healing. Design: Prospective, double-blind, multicenter, parallel-group study. Setting: Gastroenterol. practices in ambulatory and referral center settings. Patients: Three hundred fifty-three patients with an active, nonmalignant gastric ulcer at least 5 mm in diameter confirmed by endoscopy and biopsy and who continued to receive stable doses of NSAIDs. Intervention: Patients were randomized to receive ranitidine hydrochloride, 150 mg twice daily, or **lansoprazole**, 15 mg or 30 mg once daily, for 8 wk. Measurements: Healing was assessed by endoscopy at 4 and 8 wk in an intent-to-treat population. Helicobacter pylori status was assessed by histol. examination Results: After 8 wk of treatment, healing was observed in 61 (53%) of 115, 81 (69%) of 118, and 85 (73%) of 117 patients receiving ranitidine **lansoprazole**, 15 mg, and **lansoprazole**, 30 mg, resp. (P<.05 for ranitidine vs. both **lansoprazole** doses; 95% confidence interval, 3.2-28.0 for ranitidine vs. **lansoprazole**, 15 mg, and 7.4-31.8 for ranitidine vs. **lansoprazole**, 30 mg). The gastric ulcer healing rates were similar between H pylori-infected and -noninfected patients, with a statistically significant increase with the use of **lansoprazole** vs. ranitidine. Conclusions: In patients who require continuous treatment with NSAIDs, **lansoprazole** is superior to ranitidine for healing of NSAID-associated gastric ulcers. Healing is not delayed by the presence of H pylori infection.

ST **lansoprazole** ranitidine NSAID ulcer helicobacter infection

IT Antiulcer agents
Helicobacter pylori
(**lansoprazole** vs. ranitidine for healing NSAID-associated gastric ulcers and effect of H pylori infection in humans)

IT Anti-inflammatory agents
(nonsteroidal; **lansoprazole** vs. ranitidine for healing NSAID-associated gastric ulcers and effect of H pylori infection in humans)

IT Stomach, disease
(ulcer; **lansoprazole** vs. ranitidine for healing NSAID-associated gastric ulcers and effect of H pylori infection in humans)

IT 66357-35-5, Ranitidine 103577-45-3, **Lansoprazole**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**lansoprazole** vs. ranitidine for healing NSAID-associated gastric ulcers and effect of H pylori infection in humans)

L2 ANSWER 40 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:382805 CAPLUS
DOCUMENT NUMBER: 133:22290
TITLE: Stability of suspension formulations of **lansoprazole** and omeprazole stored in amber-colored plastic oral syringes
AUTHOR(S): DiGiacinto, Jennifer L.; Olsen, Keith M.; Bergman, Kimberly L.; Hoie, Eric B.
CORPORATE SOURCE: Clinical Pharmacology, Department of Biomedical and Therapeutic Sciences, University of Illinois College of Medicine at Peoria, Peoria, IL, USA
SOURCE: Annals of Pharmacotherapy (2000), 34(5), 600-605
CODEN: APHRER; ISSN: 1060-0280
PUBLISHER: Harvey Whitney Books Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB OBJECTIVE: To determine the stability of **lansoprazole** and omeprazole suspensions at ambient and refrigerated temps. using HPLC. DESIGN: The contents of **lansoprazole** and omeprazole capsules were suspended in sep. flasks containing sodium bicarbonate 8.4% to concns. of 3 and 2 mg/mL, resp. The contents of each flask were drawn into 6 amber oral syringes, with one-half of the syringes stored at 22° (ambient) and the other half at 4°. **Lansoprazole** and omeprazole concns. were determined by a stability-indicating HPLC assay at baseline and at 4, 8, 12, and 24 h, and on days 4, 7, 14, 21, 30, 45, and 60 after mixing. Both omeprazole and **lansoprazole** were considered **stable** if they retained ≥90% of the baseline drug concentration RESULTS: Omeprazole was **stable** for up to 14 days at 22° and 45 days at 4°. **Lansoprazole** was **stable** for 8 h at 22° and for 14 days at 4°. CONCLUSIONS: When compared with ambient or refrigerated storage conditions, omeprazole was **stable** for a longer duration than **lansoprazole**. Pharmacists may use these results to guide compounding and storage of proton-pump inhibitor suspensions.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Stability of suspension formulations of **lansoprazole** and omeprazole stored in amber-colored plastic oral syringes
AB OBJECTIVE: To determine the stability of **lansoprazole** and omeprazole suspensions at ambient and refrigerated temps. using HPLC. DESIGN: The contents of **lansoprazole** and omeprazole capsules were suspended in sep. flasks containing sodium bicarbonate 8.4% to concns. of 3 and 2 mg/mL, resp. The contents of each flask were drawn into 6 amber oral syringes, with one-half of the syringes stored at 22° (ambient) and the other half at 4°. **Lansoprazole** and omeprazole concns. were determined by a stability-indicating HPLC assay at baseline and at 4, 8, 12, and 24 h, and on days 4, 7, 14, 21, 30, 45, and 60 after mixing. Both omeprazole and **lansoprazole** were considered **stable** if they retained ≥90% of the baseline drug concentration RESULTS: Omeprazole was **stable** for up to 14 days at 22° and 45 days at 4°. **Lansoprazole** was **stable** for 8 h at 22° and for 14 days at 4°. CONCLUSIONS: When compared with ambient or refrigerated storage conditions, omeprazole was **stable** for a longer duration than **lansoprazole**. Pharmacists may use these results to guide compounding and storage of proton-pump inhibitor suspensions.
ST stability suspension plastic syringe **lansoprazole** omeprazole
IT Syringes
(stability of suspension formulations of **lansoprazole** and omeprazole stored in amber plastic oral syringes)
IT Polymers, uses

RL: DEV (Device component use); USES (Uses)
(stability of suspension formulations of **lansoprazole** and omeprazole stored in amber plastic oral syringes)

IT Drug delivery systems
(suspensions; stability of suspension formulations of **lansoprazole** and omeprazole stored in amber plastic oral syringes)

IT 73590-58-6, Omeprazole 103577-45-3, **Lansoprazole**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stability of suspension formulations of **lansoprazole** and omeprazole stored in amber plastic oral syringes)

L2 ANSWER 41 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:764804 CAPLUS
DOCUMENT NUMBER: 132:216466
TITLE: A rapid high-performance liquid chromatographic determination of **Lansoprazole** in human serum
AUTHOR(S): Zaater, M. F.; Najib, N.; Ghanem, E.
CORPORATE SOURCE: Department of Applied Chemical Sciences, Jordan University of Science and Technology (JUST), Irbid, Jordan
SOURCE: Saudi Pharmaceutical Journal (1999), 7(3), 123-129
CODEN: SPJOEM; ISSN: 1319-0164
PUBLISHER: Saudi Pharmaceutical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A simple and rapid reversed-phase high-performance liquid chromatog. (RP-HPLC) method with UV detection has been described for the determination of Lansoprazole in human serum. Carbamazepine was used as internal standard The drug and the internal standard in serum were extracted twice with di-Et ether, followed by evaporation, reconstitution in the mobile phase, and injection into the chromatog. system. The method utilized a Nova-Pak C18 4-μm column (150+3.9 mm i.d.) together with an isocratic mobile phase which consisted of 0.02M sodium dihydrogenphosphate-acetonitrile-methanol (58:23:19%, volume/volume/volume). The mobile phase was adjusted to pH 7.3 with 5M NaOH and pumped at a flow rate of 1.8 mL/min. The UV detector was set at 285 nm. Running time per single anal. was <4 min. The response of the assay was linear with a correlation coefficient of r=0.9993. The within and between-day coeffs. of variation for 3 different concns. (50-1500 ng/mL) ranged from 1.14 to 8.26% and from 1.66 to 8.02%, resp. The average recovery of the concentration range stated was better than 96.5%. Stability testing revealed that **Lansoprazole** was **stable** in serum at -20° for 2 wk. The method was successfully applied in a bioassay study of 2 products each in the form of enteric-coated granules in capsules containing 30 mg **Lansoprazole**, administered orally to 18 healthy male volunteers.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI A rapid high-performance liquid chromatographic determination of **Lansoprazole** in human serum

AB A simple and rapid reversed-phase high-performance liquid chromatog. (RP-HPLC) method with UV detection has been described for the determination of **Lansoprazole** in human serum. Carbamazepine was used as internal standard The drug and the internal standard in serum were extracted twice with di-Et ether, followed by evaporation, reconstitution in the mobile phase, and injection into the chromatog. system. The method utilized a Nova-Pak C18 4-μm column (150+3.9 mm i.d.) together with an isocratic mobile phase which consisted of 0.02M sodium dihydrogenphosphate-acetonitrile-

methanol (58:23:19%, volume/volume/volume). The mobile phase was adjusted to pH 7.3 with 5M NaOH and pumped at a flow rate of 1.8 mL/min. The UV detector was set at 285 nm. Running time per single anal. was <4 min. The response of the assay was linear with a correlation coefficient of r=0.9993. The within and between-day coeffs. of variation for 3 different concns. (50-1500 ng/mL) ranged from 1.14 to 8.26% and from 1.66 to 8.02%, resp. The average recovery of the concentration range stated was better than 96.5%. Stability testing revealed that **Lansoprazole** was **stable** in serum at -20° for 2 wk. The method was successfully applied in a bioassay study of 2 products each in the form of enteric-coated granules in capsules containing 30 mg **Lansoprazole**, administered orally to 18 healthy male volunteers.

ST **Lansoprazole** detn serum human HPLC; liq chromatog
Lansoprazole serum human

IT Blood analysis
(**Lansoprazole** detn in blood serum of humans by reversed-phase HPLC)

IT 103577-45-3, **Lansoprazole**
RL: ANT (Analyte); ANST (Analytical study)
(**Lansoprazole** detn in blood serum of humans by reversed-phase HPLC)

L2 ANSWER 42 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:763691 CAPLUS
DOCUMENT NUMBER: 132:6362
TITLE: A **stable** oral pharmaceutical composition containing a substituted pyridylsulfinyl benzimidazole
INVENTOR(S): Thacharodi, Dilip Kumar; Kampal, Ashok
PATENT ASSIGNEE(S): Ranbaxy Laboratories, Limited, India
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 960620	A1	19991201	EP 1998-123251		19981207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
ZA 9810765	A	19990806	ZA 1998-10765		19981125
RU 2216321	C2	20031120	RU 1998-122664		19981209
CN 1237415	A	19991208	CN 1998-125528		19981218
WO 9961022	A1	19991202	WO 1999-IB139		19990126
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
AU 9919797	A1	19991213	AU 1999-19796		19990126
BR 9910723	A	20010612	BR 1999-10723		19990126
PRIORITY APPLN. INFO.:			US 1998-86224	A	19980528
			WO 1999-IB139	W	19990126

OTHER SOURCE(S): MARPAT 132:6362

AB A pharmaceutical composition which is **stable** and suitable for oral administration to a patient comprises a mixture of a substituted pyridyl

sulfinyl benzimidazole having gastric acid secretion inhibitory activity (such as omeprazole, **lansoprazole**, or pantoprazole), and a pharmaceutically acceptable carrier. The carrier comprises a polymer having vinylpyrrolidone monomeric units, such as polyvinylpyrrolidone or a vinyl pyrrolidone-vinyl acetate copolymer. Surprisingly, it has been found that the vinylpyrrolidone polymer acts as a stabilizing excipient on the substituted pyridyl sulfinyl benzimidazole so that the composition need not include any alkaline components to prevent degradation of the active ingredient.

In a preferred embodiment, the composition is in the form of a capsule, whereby the mixture of the substituted pyridyl sulfinyl benzimidazole and the vinyl pyrrolidone polymer in the form of a powder blend or granules, is contained within a capsule shell, which capsule shell is made from an enteric material or is coated with an enteric material. Capsules were prepared containing omeprazole 20.00 and crosslinked PVP 100 mg/capsule.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI A **stable** oral pharmaceutical composition containing a substituted pyridylsulfinyl benzimidazole

AB A pharmaceutical composition which is **stable** and suitable for oral administration to a patient comprises a mixture of a substituted pyridyl sulfinyl benzimidazole having gastric acid secretion inhibitory activity (such as omeprazole, **lansoprazole**, or pantoprazole), and a pharmaceutically acceptable carrier. The carrier comprises a polymer having vinylpyrrolidone monomeric units, such as polyvinylpyrrolidone or a vinyl pyrrolidone-vinyl acetate copolymer. Surprisingly, it has been found that the vinylpyrrolidone polymer acts as a stabilizing excipient on the substituted pyridyl sulfinyl benzimidazole so that the composition need not include any alkaline components to prevent degradation of the active ingredient.

In a preferred embodiment, the composition is in the form of a capsule, whereby the mixture of the substituted pyridyl sulfinyl benzimidazole and the vinyl pyrrolidone polymer in the form of a powder blend or granules, is contained within a capsule shell, which capsule shell is made from an enteric material or is coated with an enteric material. Capsules were prepared containing omeprazole 20.00 and crosslinked PVP 100 mg/capsule.

IT Drug delivery systems
(capsules; **stable** oral pharmaceutical composition containing a substituted pyridylsulfinyl benzimidazole)

IT Drug delivery systems
(granules; **stable** oral pharmaceutical composition containing a substituted pyridylsulfinyl benzimidazole)

IT Drug delivery systems
(oral; **stable** oral pharmaceutical composition containing a substituted pyridylsulfinyl benzimidazole)

IT Gastric acid
(secretion, inhibitors; **stable** oral pharmaceutical composition containing a substituted pyridylsulfinyl benzimidazole)

IT Antacids
(**stable** oral pharmaceutical composition containing a substituted pyridylsulfinyl benzimidazole)

IT Glycerides, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** oral pharmaceutical composition containing a substituted pyridylsulfinyl benzimidazole)

IT Drug delivery systems
(tablets; **stable** oral pharmaceutical composition containing a substituted pyridylsulfinyl benzimidazole)

IT 9003-39-8, Pvp 25086-89-9, Vinyl acetate-vinylpyrrolidone copolymer
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**stable** oral pharmaceutical composition containing a substituted pyridylsulfinyl benzimidazole)

IT 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**stable** oral pharmaceutical composition containing a substituted pyridylsulfinyl benzimidazole)

L2 ANSWER 43 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:639980 CAPLUS
DOCUMENT NUMBER: 131:341883
TITLE: Effect of various salts on the stability of **lansoprazole**, omeprazole, and pantoprazole as determined by high-performance liquid chromatography
AUTHOR(S): Ekpe, Anthony; Jacobsen, Thomas
CORPORATE SOURCE: Bayer Corporation, Morristown, NJ, 07962-1910, USA
SOURCE: Drug Development and Industrial Pharmacy (1999), 25(9), 1057-1065
CODEN: DDIPD8; ISSN: 0363-9045
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A fast and reproducible reversed-phase HPLC method was developed for the simultaneous determination of omeprazole, **lansoprazole**, and pantoprazole. The 3 compds. were monitored at 280 nm by using Zorbax Eclipse XDB C8 (5 μm, 150 cm + 4.6 mm i.d.) and a mobile phase consisting of 700:300 phosphate buffer-MeCN with the pH adjusted to 7.0 with phosphoric acid. The method was used to study the effect of pH and various salts on the stability of the 3 compds. The pH rate profile curve showed that pantoprazole was the most **stable** compound and **lansoprazole** the least **stable**. The stabilities of the compds. in salt solns. were in the following order: phosphate buffer < trisodium citrate < citrate buffer ≤ acetate buffer < citric acid ≤ monosodium citrate ≤ calcium carbonate < sodium bicarbonate < sodium chloride < water. The rate of degradation had a direct relationship with the H+ and salt concentration

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Effect of various salts on the stability of **lansoprazole**, omeprazole, and pantoprazole as determined by high-performance liquid chromatography

AB A fast and reproducible reversed-phase HPLC method was developed for the simultaneous determination of omeprazole, **lansoprazole**, and pantoprazole. The 3 compds. were monitored at 280 nm by using Zorbax Eclipse XDB C8 (5 μm, 150 cm + 4.6 mm i.d.) and a mobile phase consisting of 700:300 phosphate buffer-MeCN with the pH adjusted to 7.0 with phosphoric acid. The method was used to study the effect of pH and various salts on the stability of the 3 compds. The pH rate profile curve showed that pantoprazole was the most **stable** compound and **lansoprazole** the least **stable**. The stabilities of the compds. in salt solns. were in the following order: phosphate buffer < trisodium citrate < citrate buffer ≤ acetate buffer < citric acid ≤ monosodium citrate ≤ calcium carbonate < sodium bicarbonate < sodium chloride < water. The rate of degradation had a direct relationship with the H+ and salt concentration

ST salt stability **lansoprazole** HPLC detn; omeprazole stability salt HPLC detn; pantoprazole stability salt HPLC detn; chromatog liq drug stability salt detn

IT Buffers
(salts effect on stability of **lansoprazole** and omeprazole and pantoprazole determination by HPLC)

IT Salts, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salts effect on stability of **lansoprazole** and omeprazole and pantoprazole determination by HPLC)
IT 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, Lansoprazole
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(salts effect on stability of **lansoprazole** and omeprazole and pantoprazole determination by HPLC)
IT 68-04-2, Trisodium citrate 77-92-9, Citric acid, biological studies 144-55-8, Carbonic acid monosodium salt, biological studies 471-34-1, Calcium carbonate, biological studies 7647-14-5, Sodium chloride, biological studies 18996-35-5, Monosodium citrate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salts effect on stability of **lansoprazole** and omeprazole and pantoprazole determination by HPLC)

L2 ANSWER 44 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:277794 CAPLUS
DOCUMENT NUMBER: 130:301825
TITLE: Nonaqueous capillary electrophoresis for the analysis of labile pharmaceutical compounds
AUTHOR(S): Tivesten, A.; Folestad, S.; Schonbacher, V.; Svensson, K.
CORPORATE SOURCE: Astra Hassle AB, Moelndal, S-43183, Swed.
SOURCE: Chromatographia (1999), 49(Suppl. 1), S7-S11
CODEN: CHRGB7; ISSN: 0009-5893
PUBLISHER: Friedrich Vieweg & Sohn Verlagsgesellschaft mbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A screening method using nonaq. capillary electrophoresis (NACE) has been developed for purity anal. of pyridinyl-methyl-sulfinyl-benzimidazoles (PMSB). Eight different polar organic solvents were tested as background electrolytes. N-methylformamide (NMF) was found to have the best properties in respect of both electrophoretic behavior and high solubility of five different model compds. Optimization of the CE separation with-regard to the effects of addition of various electrolyte modifiers is reported. An addnl. feature of amide solvents, rarely utilized in CE, is their intrinsic basic nature; this is of particular interest for anal. of compds. such as the PMSB, the degradation of which is acid-catalyzed. It is shown here that these compds. are **stable** at room temperature for weeks in NMF solution Results from quant. application of the NACE method were highly precise (typically 1.8% RSD for normalized peak area); linearity was good and detection limit in drug purity determination was low (.apprx.0.05 area % relative to the drug compound).
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB A screening method using nonaq. capillary electrophoresis (NACE) has been developed for purity anal. of pyridinyl-methyl-sulfinyl-benzimidazoles (PMSB). Eight different polar organic solvents were tested as background electrolytes. N-methylformamide (NMF) was found to have the best properties in respect of both electrophoretic behavior and high solubility of five different model compds. Optimization of the CE separation with-regard to the effects of addition of various electrolyte modifiers is reported. An addnl. feature of amide solvents, rarely utilized in CE, is their intrinsic basic nature; this is of particular interest for anal. of compds. such as the PMSB, the degradation of which is acid-catalyzed. It is shown here that these compds. are **stable** at room temperature for weeks in NMF solution Results from quant. application of the NACE method were highly precise (typically 1.8% RSD for normalized peak area); linearity was good and detection limit in drug purity determination was low (.apprx.0.05

area % relative to the drug compound).

ST pantoprazole **lansoprazole** omeprazole detn nonaq capillary electrophoresis; rabeprazole picoprazole detn nonaq capillary electrophoresis

IT 73590-58-6, Omeprazole 78090-11-6, Picoprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 117976-89-3, Rabeprazole
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nonaq. capillary electrophoresis for the anal. of labile pharmaceutical compds.)

L2 ANSWER 45 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:742256 CAPLUS
DOCUMENT NUMBER: 130:7429
TITLE: **Stable** oral pharmaceutical dosage forms
INVENTOR(S): Chen, Jivn-ren
PATENT ASSIGNEE(S): Sage Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9850019	A1	19981112	WO 1998-US9449	19980508
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9873755	A1	19981127	AU 1998-73755	19980508
JP 2001524131	T2	20011127	JP 1998-548544	19980508
TW 550090	B	20030901	TW 1998-87107174	19980508
US 2001006649	A1	20010705	US 1998-141476	19980827
US 6726927	B2	20040427		
US 2003203018	A1	20031030	US 2003-422338	20030424
US 2004197394	A1	20041007	US 2004-831809	20040426

PRIORITY APPLN. INFO.:

US 1997-46089P	P	19970509
US 1997-950432	A2	19971015
WO 1998-US9449	W	19980508
US 1998-141476	A3	19980827

AB The present invention relates to new **stable** enteric coated pharmaceutical dosage forms for oral use containing Omeprazole or **Lansoprazole**, to a formulation and a method for the manufacture of such a dosage form, and to a method of gastric acid pump inhibition and providing gastrointestinal cytoprotective benefit by using them. Core granulations containing omeprazole and calcium carbonate were prepared, encapsulated or directly compressed into tablets with appropriate excipients.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI **Stable** oral pharmaceutical dosage forms

AB The present invention relates to new **stable** enteric coated pharmaceutical dosage forms for oral use containing Omeprazole or **Lansoprazole**, to a formulation and a method for the manufacture of such a dosage form, and to a method of gastric acid pump inhibition and

providing gastrointestinal cytoprotective benefit by using them. Core granulations containing omeprazole and calcium carbonate were prepared, encapsulated or directly compressed into tablets with appropriate excipients.

ST oral pharmaceutical **stable**

IT Drug delivery systems
(capsules; **stable** oral pharmaceutical dosage forms)

IT Coating materials
(enteric; **stable** oral pharmaceutical dosage forms)

IT Drug delivery systems
(oral; **stable** oral pharmaceutical dosage forms)

IT Granulation
(**stable** oral pharmaceutical dosage forms)

IT Polyoxyalkylenes, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** oral pharmaceutical dosage forms)

IT Drug delivery systems
(tablets; **stable** oral pharmaceutical dosage forms)

IT 50-70-4, Sorbitol, biological studies 50-99-7, D-Glucose, biological studies 63-42-3, Lactose 69-65-8, D-Mannitol 79-41-4D, Methacrylic acid, polymers 144-55-8, Sodium bicarbonate, biological studies 151-21-3, Sodium lauryl sulfate, biological studies 471-34-1, Calcium carbonate, biological studies 557-04-0, Magnesium stearate 1327-43-1, Magnesium aluminum silicate 1592-23-0, Calcium stearate 7558-79-4, Dibasic sodium phosphate 7757-93-9, Dicalcium phosphate 7758-87-4, Tricalcium phosphate 9003-20-7, Polyvinyl acetate 9004-32-4, Sodium CM-cellulose 9004-34-6, Cellulose, biological studies 9004-38-0, Cellulose acetate phthalate 9004-53-9, Dextrin 9004-62-0, Hydroxyethyl cellulose 9004-65-3, Hpmc 9005-25-8, Starch, biological studies 9050-04-8, Calcium CM-cellulose 9050-31-1, Hydroxypropyl methyl cellulose phthalate 9050-36-6, Maltodextrin 14807-96-6, Talcum, biological studies 25322-68-3 31566-31-1, Glycerol monostearate 52907-01-4, Cellulose acetate trimellitate 71138-97-1, Hydroxypropyl methyl cellulose acetate succinate
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** oral pharmaceutical dosage forms)

IT 73590-58-6, Omeprazole 95510-70-6 95510-71-7 95510-72-8 103577-45-3, **Lansoprazole** 114801-85-3
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**stable** oral pharmaceutical dosage forms)

IT 64-17-5, Ethanol, biological studies 67-56-1, Methanol, biological studies 67-63-0, Isopropanol, biological studies 77-93-0, Triethyl citrate 141-78-6, Acetic acid ethyl ester, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**stable** oral pharmaceutical dosage forms)

L2 ANSWER 46 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:764470 CAPLUS
DOCUMENT NUMBER: 128:7393
TITLE: Spectrophotometric determination of **lansoprazole** in its dosage forms
AUTHOR(S): Meyyanathan, S. N.; Raj, J. R. Aravinda; Suresh, B.
CORPORATE SOURCE: Dept. of Pharmaceutical Chemistry, J.S.S. College of Pharmacy, Ootacamund, 643 001, India
SOURCE: Indian Drugs (1997), 34(7), 403-406
CODEN: INDRBA; ISSN: 0019-462X
PUBLISHER: Indian Drug Manufacturers' Association
DOCUMENT TYPE: Journal

LANGUAGE: English
AB A spectrophotometric method for the determination of **lansoprazole** in dosage forms was based on the use of acetyl chloride in the presence of 1% CuSO4 solution A yellowish-red chromogen formed had an absorption maximum at 478.5 nm and was **stable** for 3 h. Beer's Law was obeyed in the concentration range of 100.0 - 600.0 μg/mL. The reproducibility of the method was 99.6%-100.9%. When the drug solution was treated with the 0.3% 3-methyl-2-benzothiazolinone hydrazone reagent in the presence of 1% ceric ammonium sulfate solution in 1N H2SO4 a red solution developed, which forms the basis for another method of determination The chromogen, which had a λmax at 491 nm, was **stable** for 90 min. Beer's Law wass obeyed in the concentration range of 100.0-500.0 μg/mL. The reproducibility of the method was 99.5-101.0%.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Spectrophotometric determination of **lansoprazole** in its dosage forms
AB A spectrophotometric method for the determination of **lansoprazole** in dosage forms was based on the use of acetyl chloride in the presence of 1% CuSO4 solution A yellowish-red chromogen formed had an absorption maximum at 478.5 nm and was **stable** for 3 h. Beer's Law was obeyed in the concentration range of 100.0 - 600.0 μg/mL. The reproducibility of the method was 99.6%-100.9%. When the drug solution was treated with the 0.3% 3-methyl-2-benzothiazolinone hydrazone reagent in the presence of 1% ceric ammonium sulfate solution in 1N H2SO4 a red solution developed, which forms the basis for another method of determination The chromogen, which had a λmax at 491 nm, was **stable** for 90 min. Beer's Law wass obeyed in the concentration range of 100.0-500.0 μg/mL. The reproducibility of the method was 99.5-101.0%.
ST **lansoprazole** detn spectrophotometry
IT 103577-45-3, **Lansoprazole**
RL: ANT (Analyte); ANST (Analytical study)
(spectrophotometric determination of **lansoprazole** in dosage forms)
IT 75-36-5, Acetyl chloride 1128-67-2, 3-Methyl-2-benzothiazolinone hydrazone 7637-03-8, Ceric ammonium sulfate
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(spectrophotometric determination of **lansoprazole** in dosage forms)

L2 ANSWER 47 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:724334 CAPLUS
DOCUMENT NUMBER: 127:362535
TITLE: Study of influence of temperature and grinding on the crystalline state of **lansoprazole**
AUTHOR(S): Vrecer, F.; Kramar, A.; Curin, A.; Grcman, M.; Kotar-Jordan, B.
CORPORATE SOURCE: KRKA, d.d.,, Novo Mesto, R&D Division, Novo Mesto, 8000, Slovenia
SOURCE: Farmacevtski Vestnik (Ljubljana) (1997), 48(Pos. Stev.), 242-243
CODEN: FMVTAV; ISSN: 0014-8229
PUBLISHER: Slovensko Farmacevtsko Drustvo
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The polymorphic form B of **lansoprazole** underwent a spontaneous transformation into the **stable** form. The transformation was facilitated by temperature and applied mech. stress. Thus, in spite of a faster dissoln. rate of the form B than that of the form A, the form B cannot be used as such in the development of the dosage forms.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Study of influence of temperature and grinding on the crystalline state of

lansoprazole
AB The polymorphic form B of **lansoprazole** underwent a spontaneous transformation into the **stable** form. The transformation was facilitated by temperature and applied mech. stress. Thus, in spite of a faster dissoln. rate of the form B than that of the form A, the form B cannot be used as such in the development of the dosage forms.
ST **lansoprazole** polymorphism temp grinding
IT Crystal morphology
Grinding (size reduction)
Polymorphism (crystal)
(temperature and grinding effect on crystalline state of **lansoprazole**)
IT 103577-45-3, **Lansoprazole**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(temperature and grinding effect on crystalline state of **lansoprazole**)

L2 ANSWER 48 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:41878 CAPLUS
DOCUMENT NUMBER: 126:139481
TITLE: Nicotinamide Derivatives as a New Class of Gastric H+/K+-ATPase Inhibitors. 1. Synthesis and Structure-Activity Relationships of N-Substituted 2-(Benzhydryl- and benzylsulfinyl)nicotinamides
AUTHOR(S): Terauchi, Hideo; Tanitame, Akihiko; Tada, Keiko; Nakamura, Keiji; Seto, Yasuhiro; Nishikawa, Yoshinori
CORPORATE SOURCE: Discovery Research Laboratories, Dainippon Pharmaceutical Company Ltd., Suita, 564, Japan
SOURCE: Journal of Medicinal Chemistry (1997), 40(3), 313-321
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new series of N-Substituted 2-(benzhydryl- and benzylsulfinyl)nicotinamides were synthesized. Upon acid activation in the acidic environment of the parietal cell, these compds. are converted into their active forms, 2,3-dihydro-3-oxoisothiazolo[5,4-b]pyridines, which inhibit gastric H+/K+-ATPase. Inhibitory activities against [14C]aminopyrine accumulation stimulated by dibutyryl cAMP in isolated rabbit parietal cells in vitro and histamine-induced gastric acid secretion in pylorus-ligated rats by intraduodenal administration in vivo were evaluated, and the structure-activity relationships were examined Among the compds. synthesized, 2-[(2,4-dimethoxybenzyl)sulfinyl]-N-(4-pyridyl)nicotinamide (I) showed potent inhibitory activities in vitro and in vivo equivalent to those of omeprazole, a typical H+/K+-ATPase inhibitor. Moreover, I was much more **stable** at neutral and weakly acidic pH than omeprazole, **lansoprazole**, and pantoprazole. I 8b is considered to be a promising agent for treating acid-related gastrointestinal disorders.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB A new series of N-Substituted 2-(benzhydryl- and benzylsulfinyl)nicotinamides were synthesized. Upon acid activation in the acidic environment of the parietal cell, these compds. are converted into their active forms, 2,3-dihydro-3-oxoisothiazolo[5,4-b]pyridines, which inhibit gastric H+/K+-ATPase. Inhibitory activities against [14C]aminopyrine accumulation stimulated by dibutyryl cAMP in isolated rabbit parietal cells in vitro and histamine-induced gastric acid secretion in pylorus-ligated rats by intraduodenal administration in vivo were evaluated, and the structure-activity relationships were examined Among the compds. synthesized, 2-[(2,4-dimethoxybenzyl)sulfinyl]-N-(4-pyridyl)nicotinamide (I) showed potent inhibitory activities in vitro and

in vivo equivalent to those of omeprazole, a typical H+/K+-ATPase inhibitor. Moreover, I was much more **stable** at neutral and weakly acidic pH than omeprazole, **lansoprazole**, and pantoprazole. I 8b is considered to be a promising agent for treating acid-related gastrointestinal disorders.

L2 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:720269 CAPLUS
DOCUMENT NUMBER: 126:219
TITLE: Pharmacokinetic optimization in the treatment of gastro-esophageal reflux disease
AUTHOR(S): Hatlebakk, Jan Gunnar; Berstad, Arnold
CORPORATE SOURCE: Haukeland Hospital, University Bergen, Bergen, Norway
SOURCE: Clinical Pharmacokinetics (1996), 31(5), 386-406
CODEN: CPKNDH; ISSN: 0312-5963
PUBLISHER: Adis
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 131 refs. Gastro-esophageal reflux disease (GORD) is a very common disorder of upper gastro-intestinal motility, differing widely in severity and prognosis. Medical therapy of GORD has involved antacids, alginates, prokinetic agents and antisecretory compds., primarily H2 receptor antagonists and proton pump inhibitors. Knowledge of the pharmacokinetics of these compds. is important, to optimize the therapeutic benefit in each patient. GORD patients are often elderly and pharmacokinetics are more variable in this group. Furthermore, they often suffer from other diseases needing medical therapy and may need a combination of drugs to heal reflux esophagitis and relieve reflux symptoms. The ideal therapy for GORD will have linear pharmacokinetics, a relatively long plasma half-life (t1/2), a duration of action allowing once daily administration, and a **stable** effect independent of interactions with food, antacids and other drugs. Over-the-counter antacids and alginates are widely used, but may affect absorption of H2 receptor antagonists like cimetidine and ranitidine. Aluminum-containing antacids may, over time, cause toxicity in patients with renal insufficiency. In the treatment of GORD, cisapride presents important advantages over earlier prokinetic compds., with a longer plasma t1/2, low penetration of the blood-brain barrier and fewer adverse effects. The group of H2 receptor antagonists is still the most frequently used therapy for GORD. Linear pharmacokinetics make dose adjustments easy and safe. In individual patients, suppression of gastric secretion is related to the area under the plasma concentration-time curve (AUC), but there is wide interindividual variation in the effect of the same oral dose. Only with frequent administration and high doses will acid suppression approx. that of proton pump inhibitors. Tolerance, with loss of effect over time, however, is most pronounced in this situation. H2 receptor antagonists seem well suited for on-demand treatment of reflux symptoms, due to the rapid onset of effect and a decreased likelihood of the development of tolerance. Effervescent formulations provide more rapid absorption and almost immediate clin. effect. Cimetidine, however, causes interference with the metabolism of several other drugs in common use. In elderly patients elimination is delayed and in patients with renal insufficiency, dose redns. of all H2 receptor antagonists are recommended. The most effective medical therapy for any severity of GORD, particularly in severe esophagitis, are the proton pump inhibitors. The substituted benzimidazoles (omeprazole, **lansoprazole** and pantoprazole), are prodrugs which once trapped and activated in the acid milieu of the gastric glands potently suppress gastric secretion of acid and pepsin. Their long duration of action, more related to the slow turnover of parietal cell H+-K+ ATPase mols., allows once daily administration in most patients. Interindividual variation in bioavailability sometimes calls for higher doses or twice daily administration. Acid suppression is

closely related to the AUC. Omeprazole is prone to interaction with the metabolism of other drugs, some of which may be clin. important. Lansoprazole seems to have an earlier onset of action than omeprazole, ascribed to higher bioavailability during the first days of treatment. Proton pump inhibitors have a slow onset of action, which makes them unsuited for on-demand therapy. Clin. practice in GORD calls for the use of not one but several substances, according to the severity and symptom pattern of the patient. Pharmacokinetic optimization in the treatment of GORD is a question of selecting the most suitable substances and administration schemes within each group. Cisapride is superior to other prokinetics in terms of longer plasma t1/2 and less toxicity. Amongst H2 receptor antagonists, the more long-acting compds., ranitidine and famotidine, will improve acidity control throughout 24 h and also cause less metabolic interaction with other drugs than cimetidine. Lansoprazole has a higher bioavailability than omeprazole from the first day of therapy, resulting in the more rapid relief of symptoms. Pantoprazole may cause fewer drug interactions than other proton pump inhibitors.

AB A review with 131 refs. Gastro-esophageal reflux disease (GORD) is a very common disorder of upper gastro-intestinal motility, differing widely in severity and prognosis. Medical therapy of GORD has involved antacids, alginates, prokinetic agents and antisecretory compds., primarily H2 receptor antagonists and proton pump inhibitors. Knowledge of the pharmacokinetics of these compds. is important, to optimize the therapeutic benefit in each patient. GORD patients are often elderly and pharmacokinetics are more variable in this group. Furthermore, they often suffer from other diseases needing medical therapy and may need a combination of drugs to heal reflux esophagitis and relieve reflux symptoms. The ideal therapy for GORD will have linear pharmacokinetics, a relatively long plasma half-life (t1/2), a duration of action allowing once daily administration, and a **stable** effect independent of interactions with food, antacids and other drugs. Over-the-counter antacids and alginates are widely used, but may affect absorption of H2 receptor antagonists like cimetidine and ranitidine. Aluminum-containing antacids may, over time, cause toxicity in patients with renal insufficiency. In the treatment of GORD, cisapride presents important advantages over earlier prokinetic compds., with a longer plasma t1/2, low penetration of the blood-brain barrier and fewer adverse effects. The group of H2 receptor antagonists is still the most frequently used therapy for GORD. Linear pharmacokinetics make dose adjustments easy and safe. In individual patients, suppression of gastric secretion is related to the area under the plasma concentration-time curve (AUC), but there is wide interindividual variation in the effect of the same oral dose. Only with frequent administration and high doses will acid suppression approx. that of proton pump inhibitors. Tolerance, with loss of effect over time, however, is most pronounced in this situation. H2 receptor antagonists seem well suited for on-demand treatment of reflux symptoms, due to the rapid onset of effect and a decreased likelihood of the development of tolerance. Effervescent formulations provide more rapid absorption and almost immediate clin. effect. Cimetidine, however, causes interference with the metabolism of several other drugs in common use. In elderly patients elimination is delayed and in patients with renal insufficiency, dose redns. of all H2 receptor antagonists are recommended. The most effective medical therapy for any severity of GORD, particularly in severe esophagitis, are the proton pump inhibitors. The substituted benzimidazoles (omeprazole, **lansoprazole** and pantoprazole), are prodrugs which once trapped and activated in the acid milieu of the gastric glands potently suppress gastric secretion of acid and pepsin. Their long duration of action, more related to the slow turnover of parietal cell H+-K+ ATPase mols., allows once daily administration in most patients. Interindividual variation in bioavailability sometimes calls for higher doses or twice daily administration. Acid suppression is

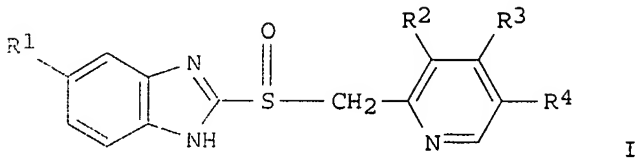
closely related to the AUC. Omeprazole is prone to interaction with the metabolism of other drugs, some of which may be clin. important. **Lansoprazole** seems to have an earlier onset of action than omeprazole, ascribed to higher bioavailability during the first days of treatment. Proton pump inhibitors have a slow onset of action, which makes them unsuited for on-demand therapy. Clin. practice in GORD calls for the use of not one but several substances, according to the severity and symptom pattern of the patient. Pharmacokinetic optimization in the treatment of GORD is a question of selecting the most suitable substances and administration schemes within each group. Cisapride is superior to other prokinetics in terms of longer plasma t1/2 and less toxicity. Amongst H2 receptor antagonists, the more long-acting compds., ranitidine and famotidine, will improve acidity control throughout 24 h and also cause less metabolic interaction with other drugs than cimetidine. **Lansoprazole** has a higher bioavailability than omeprazole from the first day of therapy, resulting in the more rapid relief of symptoms. Pantoprazole may cause fewer drug interactions than other proton pump inhibitors.

L2 ANSWER 50 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:605522 CAPLUS
DOCUMENT NUMBER: 125:230845
TITLE: New **stable** galenic formulations containing an acid-labile benzimidazole compound and their production
INVENTOR(S): Ballester Rodes, Montserrat; Van Boven, Marinus
PATENT ASSIGNEE(S): Esteve Quimica, S.A., Spain
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9623500	A1	19960808	WO 1996-ES13	19960126
W: AL, AM, AT, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE, DE, DK, DK, EE, EE, FI, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
ES 2094694	A1	19970116	ES 1995-181	19950201
ES 2094694	B1	19971216		
US 5626875	A	19970506	US 1995-429689	19950427
IL 116673	A1	20001031	IL 1996-116673	19960104
IN 186596	A	20011006	IN 1996-CA104	19960122
CA 2184842	AA	19960808	CA 1996-2184842	19960126
AU 9645403	A1	19960821	AU 1996-45403	19960126
EP 773025	A1	19970514	EP 1996-901349	19960126
EP 773025	B1	20000607		
R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, NL, PT, SE				
JP 09511257	T2	19971111	JP 1996-523278	19960126
EP 993830	A2	20000419	EP 1999-116334	19960126
EP 993830	A3	20011004		
EP 993830	B1	20050413		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, PT, IE, SI				
AT 193649	E	20000615	AT 1996-901349	19960126
ES 2148725	T3	20001016	ES 1996-901349	19960126
PT 773025	T	20001031	PT 1996-901349	19960126
DE 29623938	U1	20001109	DE 1996-29623938	19960126

TW 503115	B	20020921	TW 1996-85100946		19960126
AT 292967	E	20050415	AT 1999-116334		19960126
ZA 9600683	A	19970730	ZA 1996-683		19960130
FI 9603916	A	19960930	FI 1996-3916		19960930
PRIORITY APPLN. INFO.:			ES 1995-181	A	19950201
			EP 1996-901349	A3	19960126
			WO 1996-ES13	W	19960126

OTHER SOURCE(S): MARPAT 125:230845
GI



I

AB The title formulations comprise a neutral core on which is applied a layer containing the active ingredient (I; R1 = H, MeO, F2CHO; R2 = Me, MeO; R3 = MeO, F3CCH2O; R4 = H, Me), a water-soluble polymer, and nonalk. reaction vehicles; on this layer is applied a 2nd isolating layer which comprises a water-soluble polymer, a pigment, and talc, and a last enteric layer which contains a polymer, a plasticizer, and talc. Thus, 3010 g cores composed of sugar and starch were coated in a fluidized bed with a dispersion of omeprazole 436, hydroxypropylmethylcellulose 444, and talc 118 in H2O 3440 g. After drying, the pellets were coated with a dispersion of hydroxypropylmethylcellulose 355, talc 43, and TiO2 43 in H2O 2365 g, dried, given an enteric coating of methacrylic acid copolymer 1950, tri-Et citrate 98, and talc 98 in H2O 1890 g, dried, and stored at 40° and 75% relative humidity. Pellets stored in glass containers showed little discoloration or loss of omeprazole after 3 mo.

TI New stable galenic formulations containing an acid-labile benzimidazole compound and their production

IT Ulcer inhibitors
(stable galenic formulations containing acid-labile benzimidazole compds.)

IT Pharmaceutical dosage forms
(pellets, enteric-coated, **stable** galenic formulations containing acid-labile benzimidazole compds.)

IT 73590-58-6, Omeprazole 103577-45-3, **Lansoprazole**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable galenic formulations containing acid-labile benzimidazole compds.)

IT 9004-64-2, Hydroxypropylcellulose 9004-65-3, Hydroxypropylmethylcellulose 25086-15-1, Methacrylic acid/methyl methacrylate copolymer
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** galenic formulations containing acid-labile benzimidazole compds.)

L2 ANSWER 51 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:532133 CAPLUS
DOCUMENT NUMBER: 125:185465
TITLE: Long-term treatment with **lansoprazole** for patients with Zollinger-Ellison syndrome
AUTHOR(S): Hirschowitz, B. I.; Mohnen, J.; Shaw, S.
CORPORATE SOURCE: Department Medicine, University Alabama, Birmingham,

AL, 35294, USA
SOURCE: Alimentary Pharmacology and Therapeutics (1996), 10(4), 507-522
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Normalization of gastric secretion and cure of associated upper gastrointestinal lesions by resection of gastrinoma is possible in ≈ 20% of patients with Zollinger-Ellison syndrome, leaving ≈ 80% dependent on medical treatment with proton pump inhibitors for acid suppression. **Lansoprazole** was given for 3-48 mo (median 28 mo) to 26 Zollinger-Ellison syndrome patients with peptic ulcer manifestations in all and esophagitis in 13. Starting with 60 mg/day, the dose was individualized to lower basal acid output to less than 5 mmol/h for those with intact stomachs and less than 1 mmol/h in those who had prior gastrectomy or with esophagitis. The patients were studied every 3 mo for 1 yr and then every 6 mo with gastric anal. (basal and maximal acid and pepsin output) and endoscopy with biopsy for enterochromaffin-like (ECL) cells. **Lansoprazole** inhibited basal acid output by 95%, pepsin output by 65% and remained effective at the initial mean (66±4.3 mg/day) or smaller doses (56±12 mg/day) at 48 mo. Mucosal lesions healed and symptoms (ulcer-type pain, diarrhea, heartburn, weight loss) resolved rapidly, usually within a few weeks. Serum gastrin and ECL cell populations, which were elevated before treatment, remained statistically unchanged but one of the three multiple endocrine neoplasia I (MEN-I) patients developed a small carcinoid. Of the three patients with metastatic gastrinoma at diagnosis one has died and one has progressed, while the third has had **stable** liver metastases for 26 yr. Ulcer-type relapses occurred in three of the five post-gastrectomy patients, one with fatal jejunal ulcer perforation despite adequate acid suppression. No biochem. or clin. adverse events due to lansoprazole were encountered. **Lansoprazole** effectively inhibits acid and pepsin secretion in Zollinger-Ellison syndrome patients without any demonstrated side-effects. Despite strict acid control, post-gastrectomy Zollinger-Ellison syndrome patients were more liable to ulcer relapse, while oesophagitis was not a marker for therapeutic difficulty.

TI Long-term treatment with **lansoprazole** for patients with Zollinger-Ellison syndrome

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Ulcer-type relapses occurred in three of the five post-gastrectomy patients, one with fatal jejunal ulcer perforation despite adequate acid suppression. No biochem. or clin. adverse events due to **lansoprazole** were encountered. **Lansoprazole** effectively inhibits acid and pepsin secretion in Zollinger-Ellison syndrome patients without any demonstrated side-effects. Despite strict acid control, post-gastrectomy Zollinger-Ellison syndrome patients were more liable to ulcer relapse, while oesophagitis was not a marker for therapeutic difficulty.

ST **lansoprazole** antiulcer Zollinger Ellison syndrome; proton pump inhibitor Zollinger Ellison syndrome

IT Ulcer inhibitors
Zollinger-Ellison syndrome
(long-term treatment with **lansoprazole** for humans with Zollinger-Ellison syndrome)

IT 103577-45-3, **Lansoprazole**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(long-term treatment with **lansoprazole** for humans with Zollinger-Ellison syndrome)

L2 ANSWER 52 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:879530 CAPLUS
DOCUMENT NUMBER: 123:305840
TITLE: Review article: The continuing development of proton-pump inhibitors with particular reference to pantoprazole
AUTHOR(S): Huber, R.; Kohl, B.; Sachs, G.; Senn-Bilfinger, J.; Simon, W. A.; Sturm, E.
CORPORATE SOURCE: Research Laboratories Byk Gulden, Konstanz, D-78467, Germany
SOURCE: Alimentary Pharmacology and Therapeutics (1995), 9(4), 363-78
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 59 refs. Inhibition of the gastric proton pump is gaining acceptance as the treatment of choice for severe gastroesophageal reflux disease, and for treatment of duodenal and gastric ulceration. Three of these drugs are now available (omeprazole, **lansoprazole** and pantoprazole) and more are being developed. Proton-pump inhibitors share the same core structure, but differ in terms of substituents on this core. The substitutions are able to modify some important chemical properties of the compds. For example, pantoprazole is significantly more acid-**stable** than omeprazole or **lansoprazole**. E3810 is significantly less **stable** than the other compds. We present an explanation for this finding that depends on the relative pK values for the pyridine and benzimidazole nitrogens, especially the former. Pantoprazole formulated in an enteric-coated tablet displays high bioavailability and linear pharmacokinetics whether on single or multiple dose regimens. Although all three proton-pump inhibitors provide a similar chemical conversion to sulphenamides, which are highly reactive cysteine reagents, these reagents derivatize different cysteines in the extracytoplasmic or membrane domain of the pump and inhibit the pump at different rates. Whereas the differences in chemical reactivity can be explained by the solution chemical of the compds., selective derivatization of different cysteines on the protein argues for an involvement of pump structure in response to the presence of the proton-pump inhibitor on its luminal surface. This suggests that the proton-pump inhibitors, which were originally designed to take advantage of only the highly acidic space generated in the

parietal cell by the production of the sulphenamide, are made even more selective by the protein they target. Pantoprazole is metabolized by a combination of phase I and phase II metabolism, and has also been shown to have a very low potential for drug interaction. Studies of acid secretion in man have shown this compound to be an effective and long lasting inhibitor of acid secretion. The pharmacodynamics explain the cumulative effect of repeated doses and maximal acid secretory capacity with a once daily dosage.

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L2 ANSWER 53 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:503243 CAPLUS
DOCUMENT NUMBER: 122:248373
TITLE: Compositions for rectal administration containing benzimidazoles and fatty acid salts
INVENTOR(S): Uda, Yoshiaki
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 645140	A1	19950329	EP 1994-306401	19940831
EP 645140	B1	19981202		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2131116	AA	19950301	CA 1994-2131116	19940830
JP 07316052	A2	19951205	JP 1994-205485	19940830

US 5635520	A	19970603	US 1994-298156	19940830
CN 1106662	A	19950816	CN 1994-115636	19940831
CN 1100536	B	20030205		
AT 173924	E	19981215	AT 1994-306401	19940831
ES 2125413	T3	19990301	ES 1994-306401	19940831
PRIORITY APPLN. INFO.:			JP 1993-216685 A	19930831
			JP 1994-60972 A	19940330

OTHER SOURCE(S): MARPAT 122:248373

AB The present invention relates to a composition for rectal administration which comprises a benzimidazole compound having antiulcer activity and a salt of C6-20 fatty acid, both of which are intermingled with each other in a base for rectal administration. The composition is effective for the treatment of gastrointestinal ulcers, is excellent in the stability of the active ingredient therein and the absorption thereof to insure an early attainment of therapeutically effective blood concentration and permits control of the drug absorption rate. Furthermore, the composition swells in the intestinal tract, attaches itself to the mucosa, and releases the active ingredient gradually over a long time to supply the drug at a high concentration and with high efficiency. Therefore, the expected therapeutic efficacy can be obtained at a low dosage level with a min. side effect. A composition containing **lansoprazole** 20, PEG-4000 960, and Na oleate 20 mg was stable for >1 mo.

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ST antiulcer suppository benzimidazole fatty acid salt; rectal prepn **lansoprazole** sodium oleate stability

IT 143-19-1, Sodium oleate 408-35-5, Sodium palmitate 1002-62-6, Sodium caprate 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 103577-82-8 117976-90-6, E-3810
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rectal prepns. containing antiulcer benzimidazoles and fatty acid salts)

L2 ANSWER 54 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:294419 CAPLUS
DOCUMENT NUMBER: 122:64400
TITLE: Veterinary composition containing a proton pump inhibitor
INVENTOR(S): Olovson, Stig-Goeran Arthur; Pilbrant, Aake Gunnar
PATENT ASSIGNEE(S): Astra AB, Swed.
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9425070		A1	19941110	WO 1994-SE368	19940426
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
IL 109245		A1	20000716	IL 1994-109245	19940407
IN 182614		A	19990515	IN 1994-DE468	19940421
LT 3263		B	19950525	LT 1994-1920	19940422
CA 2161683		AA	19941110	CA 1994-2161683	19940426
AU 9466938		A1	19941121	AU 1994-66938	19940426
AU 678830		B2	19970612		
EP 696921		A1	19960221	EP 1994-914665	19940426
EP 696921		B1	20010207		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
BR 9406363		A	19960227	BR 1994-6363	19940426
CN 1122109		A	19960508	CN 1994-191967	19940426
CN 1100570		B	20030205		
JP 08509493		T2	19961008	JP 1994-524159	19940426
HU 74868		A2	19970228	HU 1995-3085	19940426
RU 2131267		C1	19990610	RU 1995-122630	19940426
CZ 285191		B6	19990616	CZ 1995-2825	19940426
PL 176755		B1	19990730	PL 1994-311276	19940426
SK 280465		B6	20000214	SK 1995-1354	19940426
AT 199060		E	20010215	AT 1994-914665	19940426
ES 2155473		T3	20010516	ES 1994-914665	19940426
PT 696921		T	20010629	PT 1994-914665	19940426
US 5731002		A	19980324	US 1994-235258	19940429
NO 9504240		A	19951023	NO 1995-4240	19951023
NO 312435		B1	20020513		
FI 9505124		A	19951027	FI 1995-5124	19951027
GR 3035831		T3	20010831	GR 2001-400679	20010507
PRIORITY APPLN. INFO.:				SE 1993-1489 A	19930430
				WO 1994-SE368 W	19940426

AB A **stable**, oral pharmaceutical composition comprising a proton pump inhibitor and a gelling agent designed for the treatment of gastric acid related diseases in animals. E.g., omeprazole enteric-coated pellets were prepared

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IT 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 104340-86-5, Leminoprazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(veterinary composition containing a proton pump inhibitor)

L2 ANSWER 55 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:491832 CAPLUS
DOCUMENT NUMBER: 121:91832
TITLE: Method for preparing a **stable** oral dosage form containing **lansoprazole**
INVENTOR(S): Moreno Rueda, Juan; Bosch Rovira, Anna; Canals Vidal, Ramon; Caldero Ges, Jose Maria
PATENT ASSIGNEE(S): Vita-Invest. S.A., Spain
SOURCE: Span., 5 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2047451	A1	19940216	ES 1992-1425	19920710
ES 2047451	B1	19941001		

PRIORITY APPLN. INFO.: ES 1992-1425 19920710

AB A stable oral dosage form for treatment of gastrointestinal illnesses [no data] can be prepared by suspending **lansoprazole** in an aqueous solution of disodium phosphate and sodium lauryl sulfate, mixing with other excipients, granulating and spherulating the mixture, and coating with a soluble isolating material and then with a final enteric coating. Filled into gelatin capsules and stored at room temperature in hermetically sealed containers, the **lansoprazole** is **stable** for 2 yr.

TI Method for preparing a **stable** oral dosage form containing **lansoprazole**

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ST lansoprazole oral dosage form formulation

IT Pharmaceutical dosage forms
(capsules, **lansoprazole**-containing, formulation of)

IT Digestive tract
(disease, **lansoprazole** oral dosage forms for treatment of, in humans)

IT 63-42-3, Lactose 69-65-8, D-Mannitol 151-21-3, Sodium lauryl sulfate, biological studies 7558-79-4, Disodium phosphate 9004-65-3, Hydroxypropylmethylcellulose 9050-31-1, Hydroxypropylmethylcellulose phthalate 36653-82-4, 1-Hexadecanol
RL: BIOL (Biological study)
(in lansoprazole-containing oral formulation)

IT 9004-34-6, Cellulose, biological studies
RL: BIOL (Biological study)
(microcryst., in **lansoprazole**-containing oral formulation)

IT 103577-45-3, **Lansoprazole**
RL: BIOL (Biological study)
(oral dosage form for human administration of, formulation of)

L2 ANSWER 56 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1994:307371 CAPLUS
DOCUMENT NUMBER: 120:307371
TITLE: Manufacturing method of **stable** enteric granules of a new antiulcer drug (**lansoprazole**)
AUTHOR(S): Tabata, Tetsuro; Makino, Tadashi; Kikuta, Junichi; Hirai, Shinichiro; Kitamori, Nobuyuki
CORPORATE SOURCE: Prod. Div., Takeda Chem. Ind., Ltd., Osaka, 532, Japan
SOURCE: Drug Development and Industrial Pharmacy (1994), 20(9), 1661-72
CODEN: DDIPD8; ISSN: 0363-9045
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the authors' previous studies, the authors clarified that enteric granules are an appropriate dosage form for **lansoprazole**, and the authors demonstrated that enteric granules could be produced when magnesium carbonate was added as an alkaline stabilizer. These granules however were found to be some unstable under severe conditions because some of the excipients are incompatible with **lansoprazole**. The

authors therefore attempted granulation not using these incompatible excipients and could obtain more **stable** enteric granules using a centrifugal fluid-bed granulator instead of an extruder-spheronizer. The authors also compared the absorption and dissoln. properties of the enteric granules manufactured by these two methods.

TI Manufacturing method of **stable** enteric granules of a new antiulcer drug (**lansoprazole**)

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ST **lansoprazole** granule enteric

IT Granulation
(of **lansoprazole**)

IT Drug bioavailability
Solution rate
(of **lansoprazole**, from enteric granules)

IT Pharmaceutical dosage forms
(granules, **lansoprazole**, manufacture of **stable** enteric)

IT 103577-45-3, **Lansoprazole**
RL: BIOL (Biological study)
(granules, manufacture of **stable** enteric)

IT 9004-64-2, Hydroxypropyl cellulose
RL: BIOL (Biological study)
(lansoprazole granules containing, manufacture of **stable** enteric)

IT 25212-88-8, Eudragit L30D-55
RL: BIOL (Biological study)
(**lansoprazole** granules enteric coated with, manufacture of **stable**)

L2 ANSWER 57 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:518333 CAPLUS
DOCUMENT NUMBER: 117:118333
TITLE: Stabilization of a new antiulcer drug (**lansoprazole**) in the solid dosage forms
AUTHOR(S): Tabata, Tetsuro; Makino, Tadashi; Kashihara, Toshio; Hirai, Shinichiro; Kitamori, Nobuyuki; Toguchi, Hajime
CORPORATE SOURCE: Pharm. Res. Lab., Takeda Chem. Ind., Ltd., Osaka, 532, Japan
SOURCE: Drug Development and Industrial Pharmacy (1992), 18(13), 1437-47
CODEN: DDIPD8; ISSN: 0363-9045
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In a previous study, the authors clarified that enteric granules were appropriate dosage forms of **lansoprazole**. The establishment of these formulations, however, was difficult because some of the excipients needed for these formulations are incompatible with the drug. The effects of adding MgCO3 as an alkaline stabilizer were examined and **stable** enteric granules were obtained. The mechanism of stabilization is also discussed.

TI Stabilization of a new antiulcer drug (**lansoprazole**) in the solid dosage forms

AB In a previous study, the authors clarified that enteric granules were

appropriate dosage forms of **lansoprazole**. The establishment of these formulations, however, was difficult because some of the excipients needed for these formulations are incompatible with the drug. The effects of adding MgCO3 as an alkaline stabilizer were examined and **stable** enteric granules were obtained. The mechanism of stabilization is also discussed.

ST lansoprazole stabilization solid dosage form; enteric granule stabilization **lansoprazole**

IT Kinetics of decomposition
(of **lansoprazole**, drug stabilization in dosage forms in relation to)

IT Pharmaceutical dosage forms
(granules, enteric-coated, **lansoprazole** stabilization in)

IT Drug interactions
(physicochem., of **lansoprazole**, with excipients)

IT Pharmaceutical dosage forms
(solids, **lansoprazole** stabilization in)

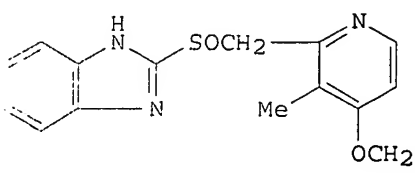
IT 57-50-1, Sucrose, biological studies 63-42-3, Lactose 557-04-0, Magnesium stearate 9003-39-8, Poly(vinylpyrrolidone) 9004-34-6, Cellulose, biological studies 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9005-25-8, Starch, biological studies 9050-04-8 13463-67-7, Titanium dioxide, biological studies 25322-68-3 106392-12-5
RL: BIOL (Biological study)
(**lansoprazole** compatibility with, in dosage forms)

IT 103577-45-3, **Lansoprazole**
RL: PROC (Process)
(stabilization of, in solid dosage forms)

IT 144-55-8, Sodium bicarbonate, biological studies 471-34-1, Calcium carbonate, biological studies 497-19-8, Sodium carbonate, biological studies 546-93-0, Magnesium carbonate 584-08-7, Potassium carbonate 1309-42-8, Magnesium hydroxide 1309-48-4, Magnesium oxide, biological studies 7487-88-9, Magnesium sulfate, biological studies 7786-30-3, Magnesium chloride, biological studies 10043-52-4, Calcium chloride, biological studies
RL: BIOL (Biological study)
(stabilizer, for **lansoprazole** granules)

L2 ANSWER 58 OF 58 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:181047 CAPLUS
DOCUMENT NUMBER: 116:181047
TITLE: Formulation studies of an acid-unstable antiulcer drug, **lansoprazole**
AUTHOR(S): Hirai, Shinichiro
CORPORATE SOURCE: Res. Dev. Div., Takeda Chem. Ind., Ltd., Osaka, 532, Japan
SOURCE: Pharm Tech Japan (1992), 8(2), 213-19
CODEN: PTJAE9; ISSN: 0910-4739
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI



I

AB **Lansoprazole** (I), a new substituted benzimidazole, is a highly specific inhibitor of gastric (H+ + K+)-ATPase. Since this compound is practically insol. in water and unstable in the acidic conditions, it is necessary to design dosage forms for improving bioavailability. From the relationship between the gastric pH and the absorption, development of an enteric dosage form was necessary to protect the degradation in the stomach. Enteric granules had better absorption properties than an enteric tablet. Moreover, by the addition of MgCO3, as an alkaline stabilizer, and by the manufacturing method using a centrifugal fluid-bed granulator instead of an extruder-spheronizer, very **stable** enteric granules were obtained. Also, I capsule containing enteric granules showed good absorption properties in human.

TI Formulation studies of an acid-unstable antiulcer drug, **lansoprazole**

AB **Lansoprazole** (I), a new substituted benzimidazole, is a highly specific inhibitor of gastric (H+ + K+)-ATPase. Since this compound is practically insol. in water and unstable in the acidic conditions, it is necessary to design dosage forms for improving bioavailability. From the relationship between the gastric pH and the absorption, development of an enteric dosage form was necessary to protect the degradation in the stomach. Enteric granules had better absorption properties than an enteric tablet. Moreover, by the addition of MgCO3, as an alkaline stabilizer, and by the manufacturing method using a centrifugal fluid-bed granulator instead of an extruder-spheronizer, very **stable** enteric granules were obtained. Also, I capsule containing enteric granules showed good absorption properties in human.

ST **lansoprazole** enteric granule capsule

IT Gastric juice
(**lansoprazole** degradation in, enteric granules for protection against)

IT Drug bioavailability
(of lan**soprazole**, from enteric granules in capsules, in humans)

IT Pharmaceutical dosage forms
(capsules, containing **lansoprazole** enteric granules, formulation and evaluation of)

IT Granulation
(fluidized-bed, of **lansoprazole**, for enteric formulation)

IT Pharmaceutical dosage forms
(granules, enteric, of **lansoprazole**, formulation and evaluation of)

IT 103577-45-3, **Lansoprazole**
RL: BIOL (Biological study)
(capsules containing enteric granules of, formulation and evaluation of)

IT 546-93-0, Magnesium carbonate
RL: BIOL (Biological study)
(stabilizer, for **lansoprazole** enteric granules)

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